



# ***STIC Search Report***

## ***Biotech-Chem Library***

**STIC Database Tracking Number: 182692**

**TO: Marcela Cordero Garcia**  
**Location: REM/3A30/3C18**  
**Art Unit: 1654**  
**March 22, 2006**

**Case Serial Number: 10/802013**

**From: P. Sheppard**  
**Location: Remsen Building**  
**Phone: (571) 272-2529**

**sheppard@uspto.gov**

### **Search Notes**

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Cordero Garcia 10\_802013 - - History

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FILE 'REGISTRY' ENTERED AT 12:21:18 ON 22 MAR 2006

L1 STR  
L2 STR  
L3 1666 SEA SSS FUL L1 OR L2  
L8 STR  
L22 STR  
L23 2 SEA SUB=L3 SSS FUL L8 AND L22

FILE 'HCAPLUS' ENTERED AT 12:45:18 ON 22 MAR 2006

L27 6 SEA ABB=ON PLU=ON L23  
D STAT QUE  
D IBIB ABS HITSTR L27 1-6

FILE 'REGISTRY' ENTERED AT 12:46:14 ON 22 MAR 2006

L28 STR  
L29 STR  
L30 5 SEA SUB=L3 SSS FUL L28 OR L29  
L31 5 SEA ABB=ON PLU=ON L30 NOT L23

FILE 'HCAPLUS' ENTERED AT 12:53:34 ON 22 MAR 2006

L32 1 SEA ABB=ON PLU=ON L31  
L33 1 SEA ABB=ON PLU=ON L32 NOT L27  
D STAT QUE L33  
D IBIB ABS HITSTR L33 1

FILE 'REGISTRY' ENTERED AT 12:56:10 ON 22 MAR 2006

L39 STR L28  
L40 STR L29  
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L42 8 SEA ABB=ON PLU=ON L41 NOT (L23 OR L31)

FILE 'HCAPLUS' ENTERED AT 12:58:52 ON 22 MAR 2006

L43 6 SEA ABB=ON PLU=ON L42  
L44 6 SEA ABB=ON PLU=ON L43 NOT (L27 OR L33)  
D STAT QUE  
D IBIB ABS HITSTR L44 1-6  
L45 49 SEA ABB=ON PLU=ON "MOLINO B"/AU OR "MOLINO B F"/AU OR  
("MOLINO BRUCE"/AU OR "MOLINO BRUCE F"/AU OR "MOLINO BRUCE  
FRANCIS"/AU)  
L46 21 SEA ABB=ON PLU=ON ("HAYDAR S"/AU OR "HAYDAR S N"/AU) OR  
"HAYDAR SIMON"/AU OR "HAYDAR SIMON N"/AU  
L47 9 SEA ABB=ON PLU=ON ("HEMENWAY MICHAEL S"/AU OR "HEMENWAY  
MICHAEL SCOTT"/AU)  
L49 76 SEA ABB=ON PLU=ON L45 OR L46 OR L47  
L50 563 SEA ABB=ON PLU=ON "YANG Z"/AU OR YANG ZHICAI?/AU  
L51 105 SEA ABB=ON PLU=ON "RICH JOSEPH"/AU OR ("RICH JOSEPH O"/AU OR  
"RICH JOSEPH OSWALD"/AU) OR RICH J/AU OR RICH J O/AU  
L52 1 SEA ABB=ON PLU=ON L50 AND L51  
L54 22554 SEA ABB=ON PLU=ON L3 OR ?CYCLOSPOR?  
L55 5 SEA ABB=ON PLU=ON (L50 OR L51) AND L54  
L56 77 SEA ABB=ON PLU=ON (L49 OR L52 OR L55) NOT (L33 OR L27)  
D STAT QUE L56  
D IBIB ABS L56 1-77

FILE 'REGISTRY' ENTERED AT 13:12:01 ON 22 MAR 2006

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FILE HOME

FILE REGISTRY

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 21 MAR 2006 HIGHEST RN 877591-95-2

DICTIONARY FILE UPDATES: 21 MAR 2006 HIGHEST RN 877591-95-2

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

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*****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005. A new display format, IDERL, is now      *
* available and contains the CA role and document type information.  *
*
*****
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Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

FILE HCAPLUS

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FILE COVERS 1907 - 22 Mar 2006 VOL 144 ISS 13

FILE LAST UPDATED: 21 Mar 2006 (20060321/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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=> fil hcaplus  
 FILE 'HCAPLUS' ENTERED AT 12:45:18 ON 22 MAR 2006  
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 PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

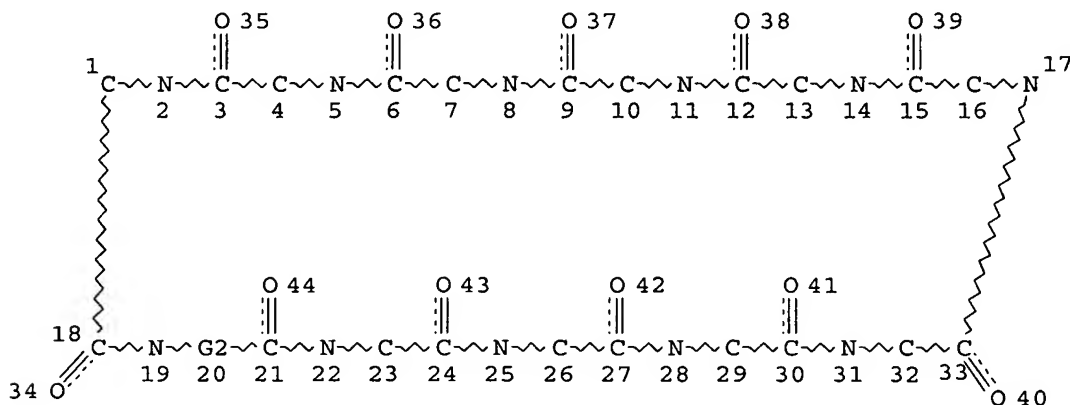
FILE COVERS 1907 - 22 Mar 2006 VOL 144 ISS 13  
 FILE LAST UPDATED: 21 Mar 2006 (20060321/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=>  
 =>

=> d stat que  
 L1 STR



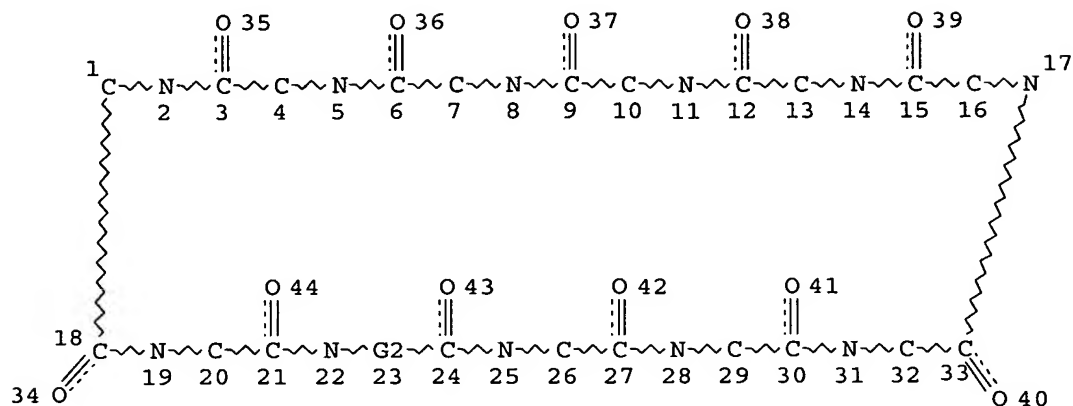
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 @45 46      @47 48 @49

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 DEFAULT MLEVEL IS ATOM  
 DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
 RING(S) ARE ISOLATED OR EMBEDDED  
 NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L2 STR



CH<sup>^</sup>CH3 CH2·CH2·CH2  
@45 46 @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

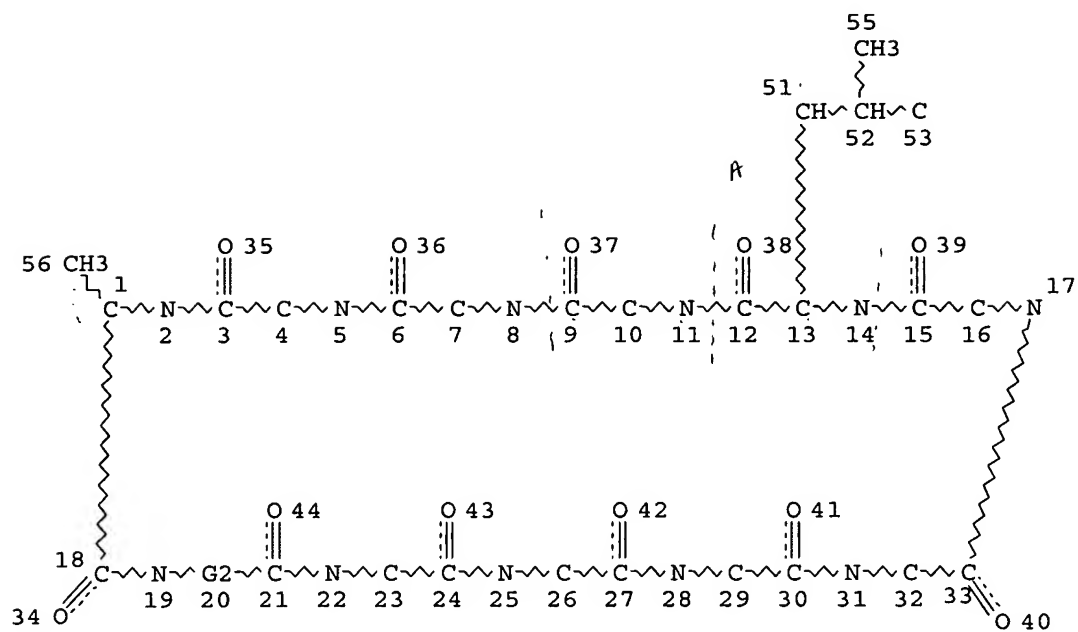
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L3 1666 SEA FILE=REGISTRY SSS FUL L1 OR L2

L8 STR





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VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

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DEFAULT ECLEVEL IS LIMITED

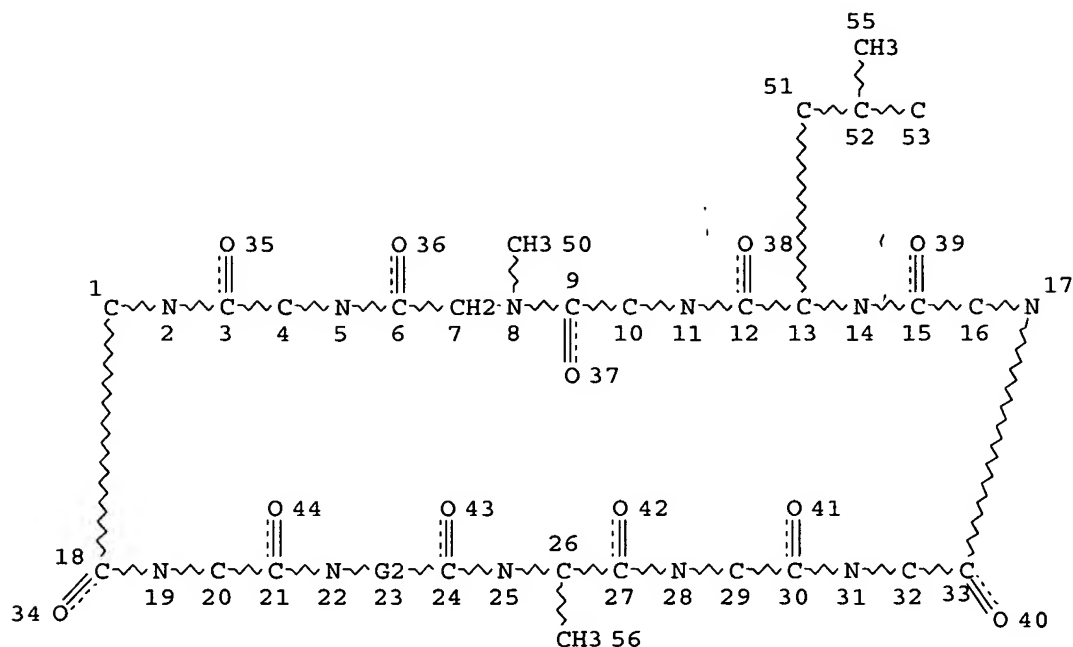
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NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE

L22              STR



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@45 46      @47 48 @49

VAR G2=45/47-22 49-24  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE  
L23            2 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 AND L22  
L27            6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

=>  
=>

=> d ibib abs hitstr l27 1-6

L27 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN  
ACCESSION NUMBER: 1994:475261 HCAPLUS  
DOCUMENT NUMBER: 121:75261  
TITLE: Human Cyclophilin C: Primary Structure, Tissue  
Distribution, and Determination of Binding Specificity  
for Cyclosporins  
AUTHOR(S): Schneider, Helmut; Charara, Nadine; Schmitz, Rita;  
Wehrli, Susi; Mikol, Vincent; Zurini, Mauro G. M.;  
Quesniaux, Valerie F. J.; Movva, N. Rao  
CORPORATE SOURCE: Sandoz Pharma Ltd., Basel, CH-4002, Switz.

SOURCE: Biochemistry (1994), 33(27), 8218-24  
 CODEN: BICHAW; ISSN: 0006-2960  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

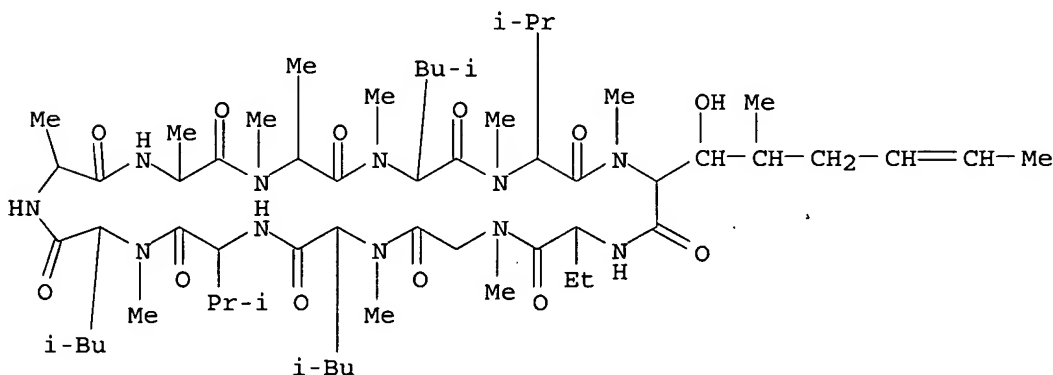
AB A cDNA for human cyclophilin C (Cyp-C) was isolated from a human kidney cDNA library. Northern blot expts. with several human tissues and cell lines revealed that Cyp-C is less abundant than Cyp-A. The amount of Cyp-C mRNA was 10-fold lower than that of Cyp-A in kidney. Expression of human Cyp-C in the kidney is not significantly elevated compared to pancreas, skeletal muscle, heart, lung, and liver. This argues against a previously postulated specific role for Cyp-C in the nephrotoxic effects of CsA in humans, based on the studies of its relative abundance in murine kidney. It is present in extremely low concns. in brain and in the Jurkat T cell line. The binding of recombinant human Cyp-A, -B, and -C to cyclosporin A (CsA) was studied by immunochem. methods. The relative affinity of Cyp-C for CsA is lower by a factor of 2 than that of Cyp-A, which itself is 10-fold lower than that of Cyp-B. Cross-reactivity studies with a series of Cs derivs. showed that Cyp-C binds CsA with a fine specificity similar to that of Cyp-A and Cyp-B. Cs amino acid residues 1, 2, 10, and 11 seemed essential for the interaction with all three Cyp subtypes. However, Cyp-C tolerates a greater variety of structures on Cs position 2 than Cyp-A does, suggesting that this residue of CsA might not be in tight contact with Cyp-C. This was confirmed by modeling of human Cyp-C on the structure of the complex formed by Cyp-A and CsA. The knowledge of the fine specificity of human CyPs for CsA and of their expression levels may provide better insights into how CsA acts on its different target proteins in vivo.

IT 112067-18-2

RL: BIOL (Biological study)  
 (cyclophilin C and A and B binding specificity for, of human)

RN 112067-18-2 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:199063 HCAPLUS

DOCUMENT NUMBER: 114:199063

TITLE: Is cyclophilin involved in the immunosuppressive and nephrotoxic mechanism of action of cyclosporin A?

AUTHOR(S): Sigal, Nolan H.; Dumont, Francis; Durette, Philippe; Siekierka, John J.; Peterson, Laurence; Rich, Daniel H.; Dunlap, Brian E.; Staruch, Marie J.; Melino, Michael R.; et al.

CORPORATE SOURCE: Dep. Immunol. Res., Merck, Sharp and Dohme Res. Lab.,

SOURCE: Rahway, NJ, 07065, USA  
Journal of Experimental Medicine (1991), 173(3),  
619-28  
CODEN: JEMEA; ISSN: 0022-1007  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The major cytosolic protein for cyclosporin A (CsA), cyclophilin, may be directly involved in mediating the immunosuppressive activity of this drug. Inhibition of the related peptidyl-prolyl cis-trans isomerase (PPIase) may inhibit murine T-cell activation. The nephrotoxicity observed with CsA may also be related to inhibition of PPIase-dependent pathways in cells other than lymphocytes. Using a series of 61 cyclosporin analogs, a good correlation was found between cyclophilin binding and immunosuppressive activity for most analogs. A number of compds. of distinct structural classes interact with cyclophilin, but were much less immunosuppressive than expected. The inability of these analogs to inhibit lymphocyte activation could not be explained by their failure to enter the cell and bind to cyclophilin under the conditions used in the cellular assays. The nonimmunosuppressive analog MeAla-6, which bound well to cyclophilin and was active as a PPIase inhibitor, did not induce any renal pathol. in vivo. The analog MeBm2t, which was immunosuppressive in vitro, possessed little or no activity as a PPIase inhibitor. These findings pose serious questions concerning the role of cyclophilin in mediating CsA immunosuppressive and nephrotoxic activities. They raise doubts about whether PPIase has a direct function in lymphocyte signal transduction.

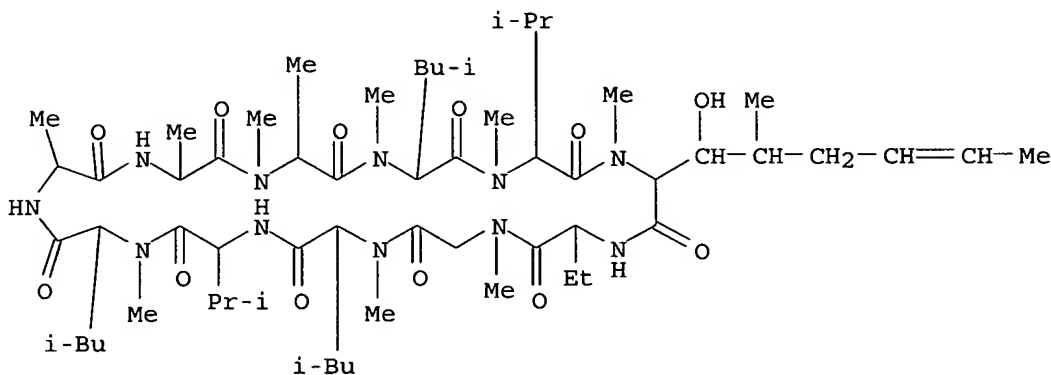
IT 112067-18-2

RL: PRP (Properties)

(immunosuppressant and nephrotoxic effects of, cyclophilin binding and structure in relation to)

RN 112067-18-2 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:542019 HCAPLUS

DOCUMENT NUMBER: 109:142019

TITLE: A study of the correlation between cyclophilin binding and in vitro immunosuppressive activity of cyclosporin A and analogs

AUTHOR(S): Durette, P. L.; Boger, J.; Dumont, F.; Firestone, R.; Frankshun, R. A.; Koprak, S. L.; Lin, C. S.; Melino, M. R.; Pessolano, A. A.; et al.

CORPORATE SOURCE: Dep. Immunol., Merck Sharp and Dohme Res. Lab.,

SOURCE: Rahway, NJ, USA  
Transplantation Proceedings (1988), 20(2, Suppl. 2),  
51-7  
CODEN: TRPPA8; ISSN: 0041-1345

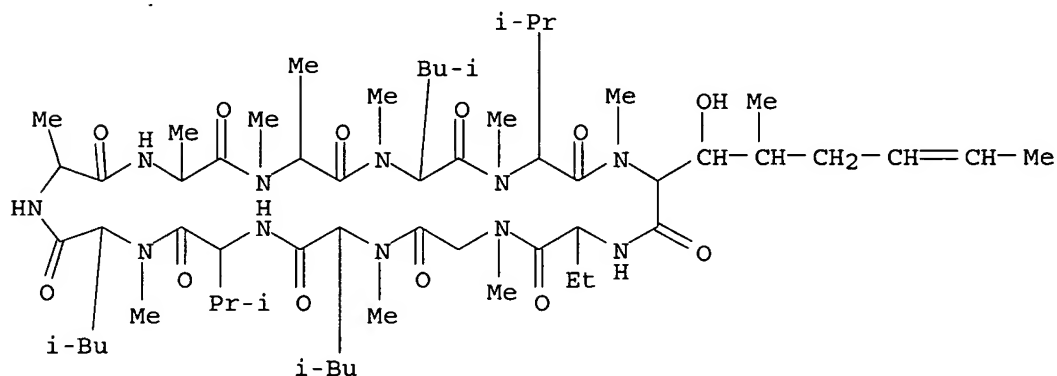
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB To establish whether cyclophilin (CyP) is the pharmacol. relevant cyclosporine A (CsA) receptor, the CyP binding vs. immunosuppressive activity was measured for an extensive, structurally varied group of CsA analogs. Overall, CyP binding paralleled immunosuppressive activity. Other than MeAla6-CsA, the few exceptions to the correlation could be ascribed to cellular metabolism. These results strongly implicate CyP or a related protein in the mechanism of action of cyclosporin.

IT 112067-18-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and cyclophilin binding and immunosuppressive activity of)

RN 112067-18-2 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:143029 HCAPLUS

DOCUMENT NUMBER: 108:143029

TITLE: Cyclophilin binds to the region of cyclosporine involved in its immunosuppressive activity

AUTHOR(S): Quesniaux, Valerie F. J.; Schreier, Max H.; Wenger, Roland M.; Hiestand, Peter C.; Harding, Matthew W.; Van Regenmortel, Marc H. V.

CORPORATE SOURCE: Lab. Immunochim., Inst. de Biol. Mol. Cell.,  
Strasbourg, F-67084, Fr.

SOURCE: European Journal of Immunology (1987), 17(9), 1359-65  
CODEN: EJIMAF; ISSN: 0014-2980

DOCUMENT TYPE: Journal  
LANGUAGE: English

AB In the present study, a quant. immunoassay for cyclophilin was developed which made it possible to compare its relative affinity for cyclosporine and any of its analogs. The binding of cyclophilin to cyclosporine coated on a solid phase was revealed by anticyclophilin rabbit antiserum followed by antiglobulin-enzyme conjugate. This reaction was inhibited by addition of free cyclosporine or certain cyclosporine analogs. By studying the binding of cyclophilin to more than 50 cyclosporine derivs. modified singly on each of the 11 amino acid residues, it was shown that cyclophilin binds to the residues of cyclosporine known to be critical for its immunosuppressive activity. Thus, cyclophilin as a highly

discriminating stereospecific binding protein for cyclosporine.

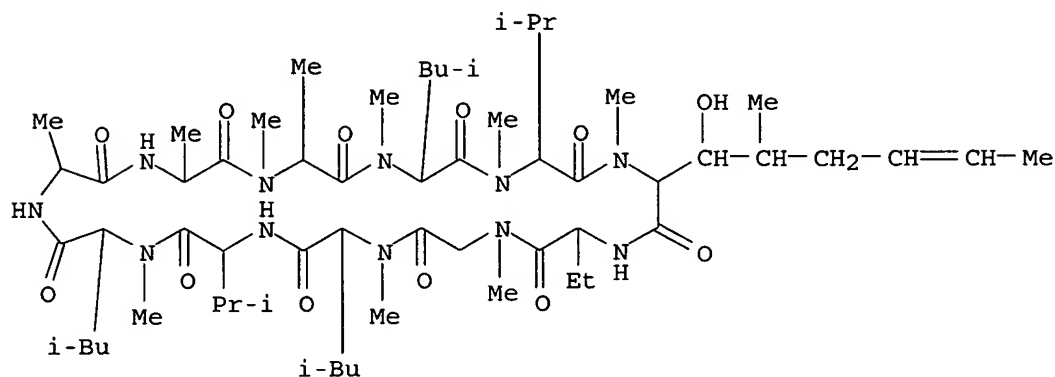
IT 105300-13-8

RL: BIOL (Biological study)

(cyclophilin binding to, specificity of, immunosuppression in relation to)

RN 105300-13-8 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-D-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:36050 HCAPLUS

DOCUMENT NUMBER: 108:36050

TITLE: Fine specificity and cross-reactivity of monoclonal antibodies to cyclosporine

AUTHOR(S): Quesniaux, Valerie F. J.; Tees, Reet; Schreier, Max H.; Wenger, Roland M.; Van Regenmortel, Marc H. V.

CORPORATE SOURCE: Sandoz Ltd., Basel, CH-4002, Switz.

SOURCE: Molecular Immunology (1987), 24(11), 1159-68

CODEN: MOIMD5; ISSN: 0161-5890

DOCUMENT TYPE: Journal

LANGUAGE: English

AB More than 180 monoclonal antibodies (McAbs) to the cyclic undecapeptide cyclosporine (Cs) have been prepared. Several immunization protocols and antibody screening processes were compared. Two main groups of McAbs recognizing different sides of the Cs mol. could be differentiated. The antibodies belonged to the IgG and IgA classes and showed high affinity for Cs. Based on their ability to discriminate Cs-derivs. modified singly at each of the 11 residues of the Cs mol., the antigenic recognition pattern of different McAbs was studied at the level of individual residues. Closely related recognition patterns were found in each of the 2 main McAb groups. The apparent size of the Cs antigenic sites recognized by different McAbs varied from 4-10 residues and did not correlate with antibody affinity.

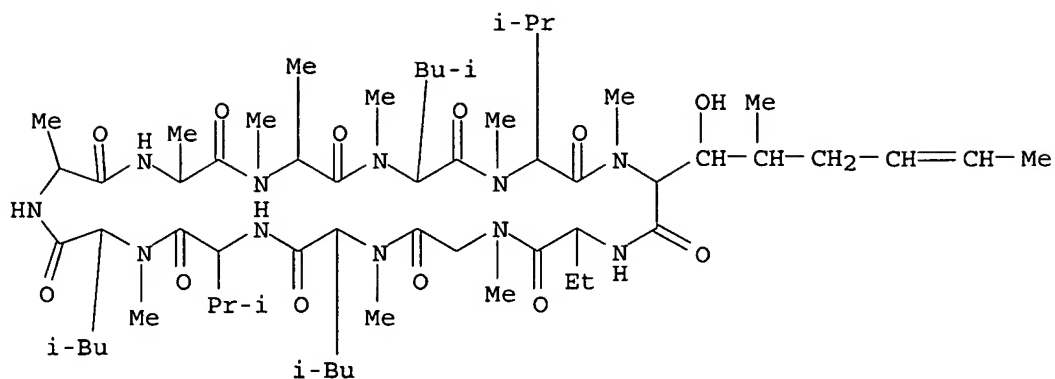
IT 112067-18-2

RL: BIOL (Biological study)

(cyclosporine-specific monoclonal antibodies cross-reactivity with)

RN 112067-18-2 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-L-alanine)- (9CI) (CA INDEX NAME)



L27 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:618544 HCAPLUS

DOCUMENT NUMBER: 105:218544

TITLE: Fine specificity of monoclonal antibodies by cyclosporine

AUTHOR(S): Quesniaux, V.; Tees, R.; Schreier, M. H.; Wenger, R. M.; Van Regenmortel, M. H. V.

CORPORATE SOURCE: Preclin. Res., Sandoz Ltd., Basel, CH-4002, Switz.

SOURCE: Transplantation Proceedings (1986), 18(4), 777-9  
CODEN: TRPPA8; ISSN: 0041-1345

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reactivity of monoclonal antibodies to cyclosporine with 50 cyclosporine derivs. was tested. The monoclonal antibodies were found to discriminate between chemical defined cyclosporine derivs. showing only minor structural changes.

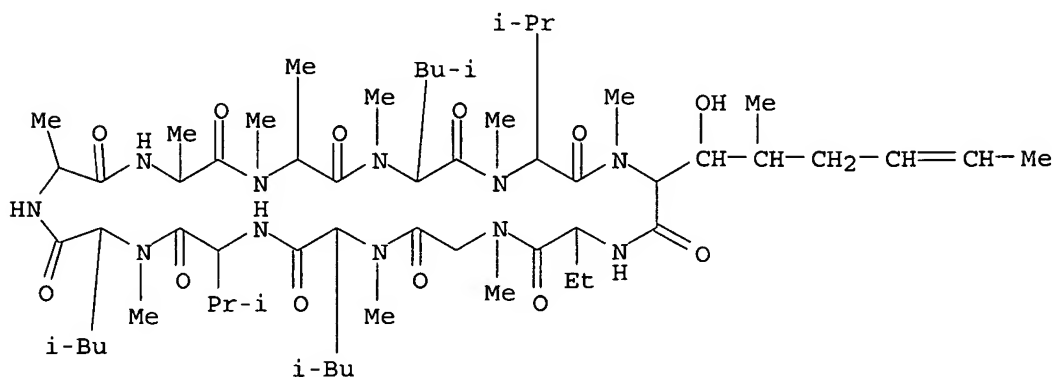
IT 105300-13-8

RL: BIOL (Biological study)

(monoclonal antibodies to cyclosporine reactivity with)

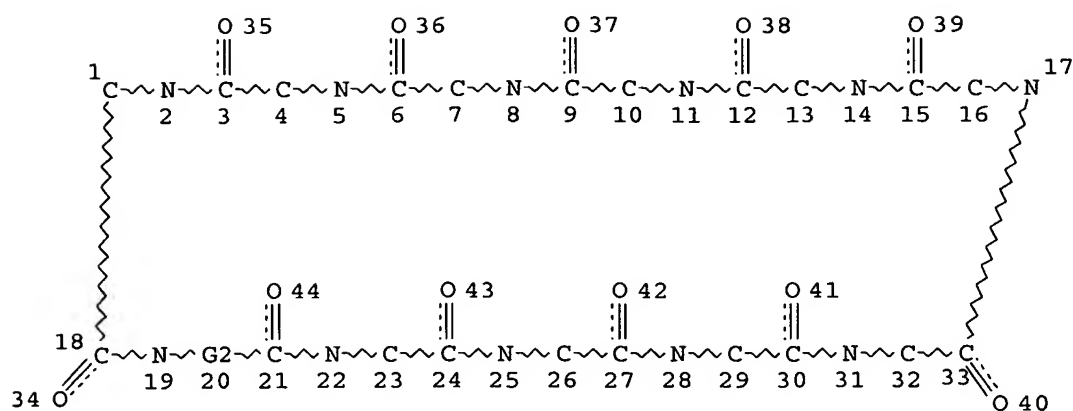
RN 105300-13-8 HCAPLUS

CN Cyclosporin A, 3-(N-methyl-D-alanine)- (9CI) (CA INDEX NAME)



=> => d stat que 133

L1 STR



CH $\searrow$ CH<sub>3</sub>      CH<sub>2</sub>·CH<sub>2</sub>·CH<sub>2</sub>  
 @45 46      @47 48 @49

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

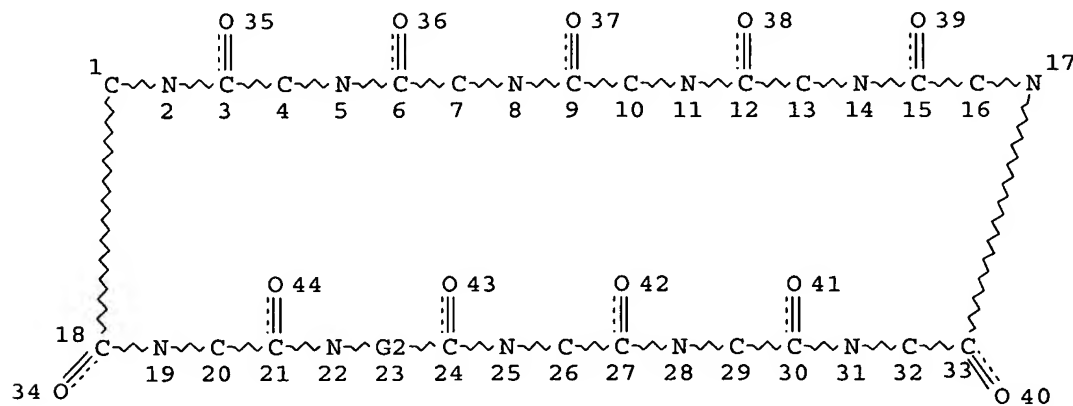
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RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L2                      STR



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 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

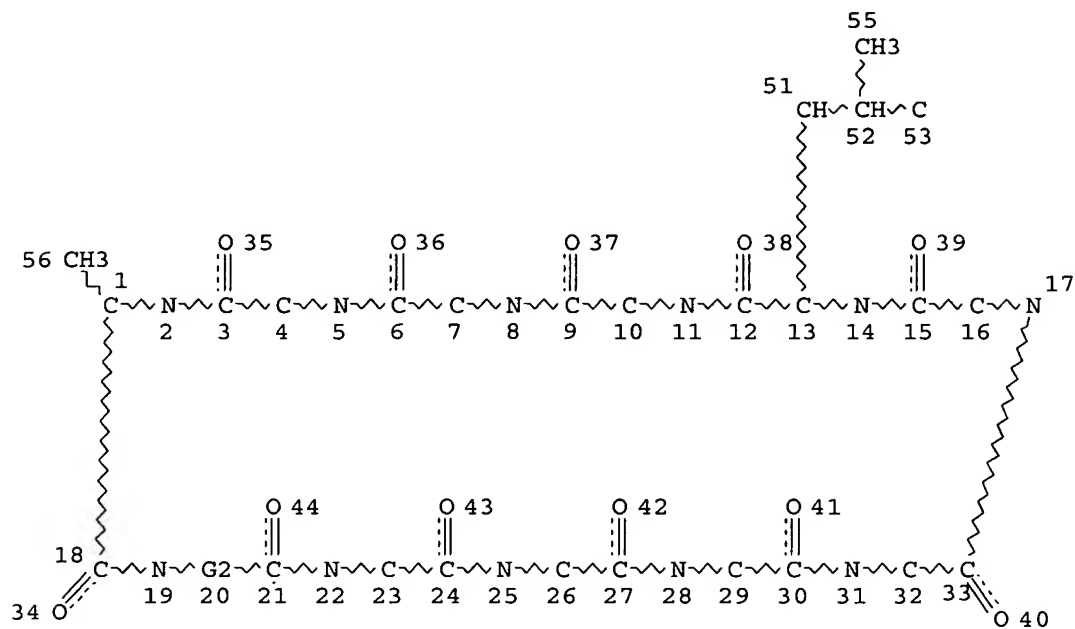


GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L3 1666 SEA FILE=REGISTRY SSS FUL L1 OR L2  
L8 STR



CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

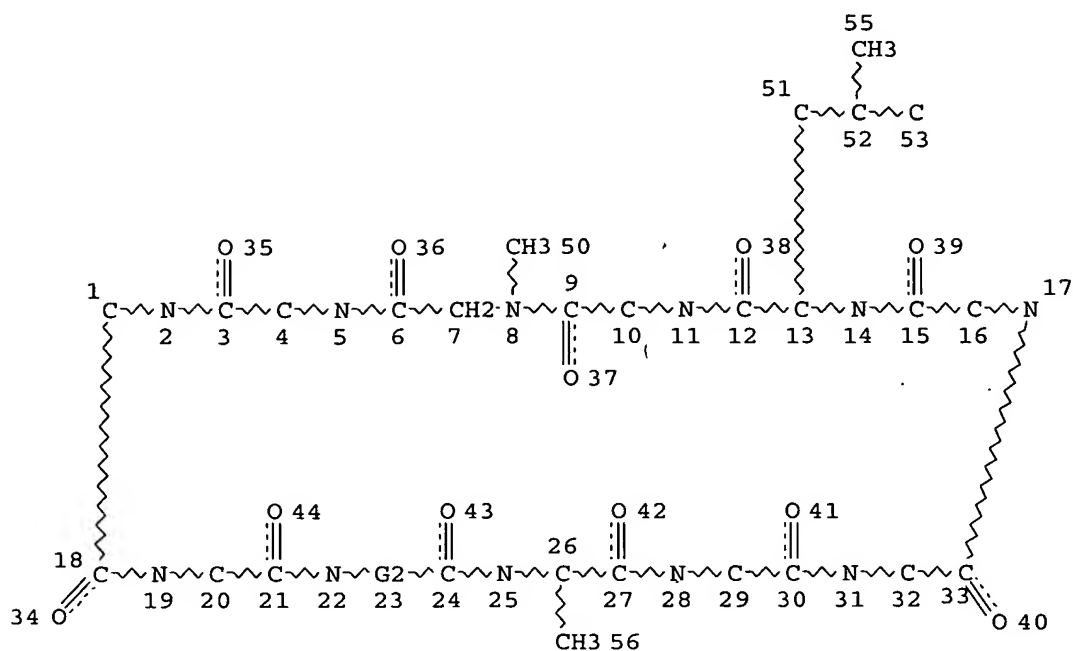
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE

L22 STR



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@45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

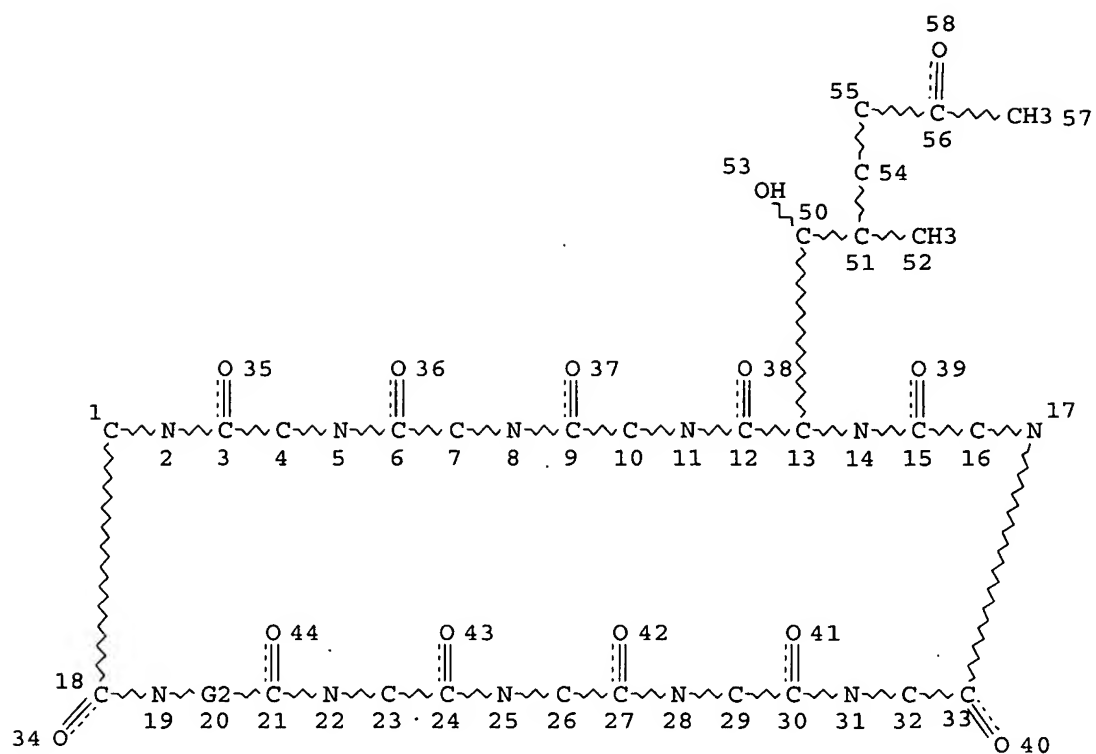
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L23      2 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 AND L22

L27      6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

L28      STR



Page 1-A

CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

Page 2-A

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

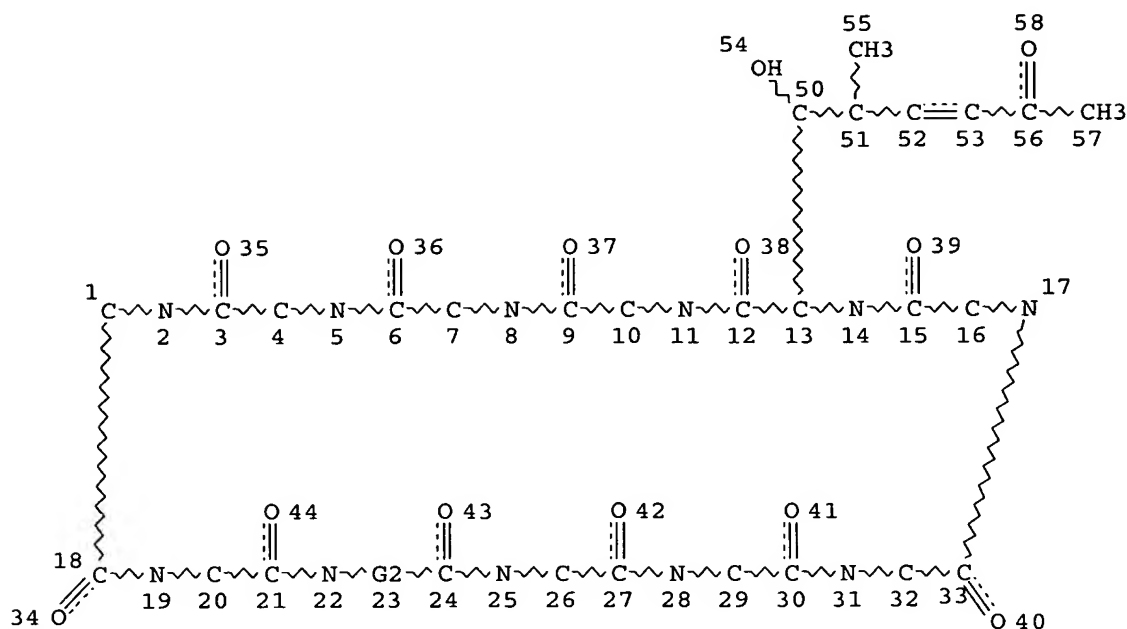
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RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L29      STR



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 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L30            5 SEA FILE=REGISTRY SUB=L3 SSS FUL L28 OR L29

L31            5 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L23

L32            1 SEA FILE=HCAPLUS ABB=ON PLU=ON L31

L33            1 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L27

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L33 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:799453 HCAPLUS

DOCUMENT NUMBER: 141:296297

TITLE: Preparation of novel cyclosporins

INVENTOR(S): Molino, Bruce F.; Haydar, Simon N.; Yang, Zhicai;  
 Michels, Peter C.; Hemenway, Michael S.; Rich, Joseph  
 O.; Khmel'nitsky, Yuri

PATENT ASSIGNEE(S): Albany Molecular Research, Inc., USA

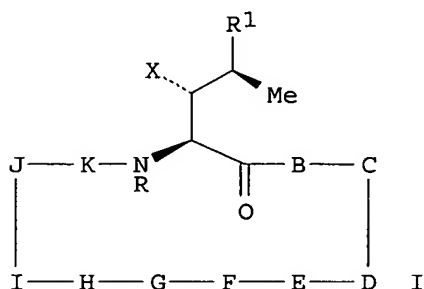
SOURCE: PCT Int. Appl., 249 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004082629	A2	20040930	WO 2004-US8118	20040316
WO 2004082629	A3	20051201		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2518265	AA	20040930	CA 2004-2518265	20040316
US 2004235716	A1	20041125	US 2004-802013	20040316
EP 1603512	A2	20051214	EP 2004-757551	20040316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK				
PRIORITY APPLN. INFO.:			US 2003-455727P	P 20030317
			WO 2004-US8118	W 20040316
OTHER SOURCE(S):		MARPAT 141:296297		
GI				



AB The invention relates cyclic peptides I [X is H, OH or a hydroxy group derivatized with an alkanoyl, aryloyl, alkyl-, aryl- or arylalkylaminocarbonyl or -oxycarbonyl group; R is H or Me; R1 is H, CHO, CH:CHCOMe, etc.; B, C, D, E, F, G, H, I, J, and K are certain amino acid residues] or their pharmaceutically-acceptable salts. Thus, cyclosporin A was converted to cyclosporin A Me vinyl ketone [R1 = (E)-2-butenyl to R1 = (E)-3-oxo-1-butenyl] by a biocatalytic method (HOBt-mediated laccase oxidation) or chemical methods using N-hydroxyphthalimide and benzoyl peroxide or tert-Bu hydroperoxide and sodium periodate.

IT **761448-79-7P**

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

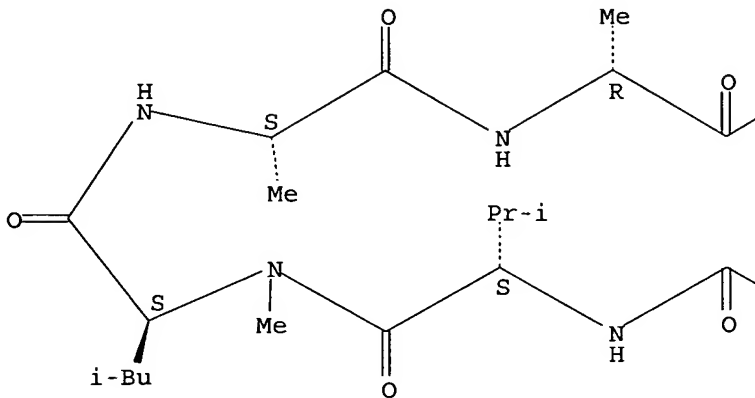
(preparation of novel cyclosporins)

RN 761448-79-7 HCAPLUS

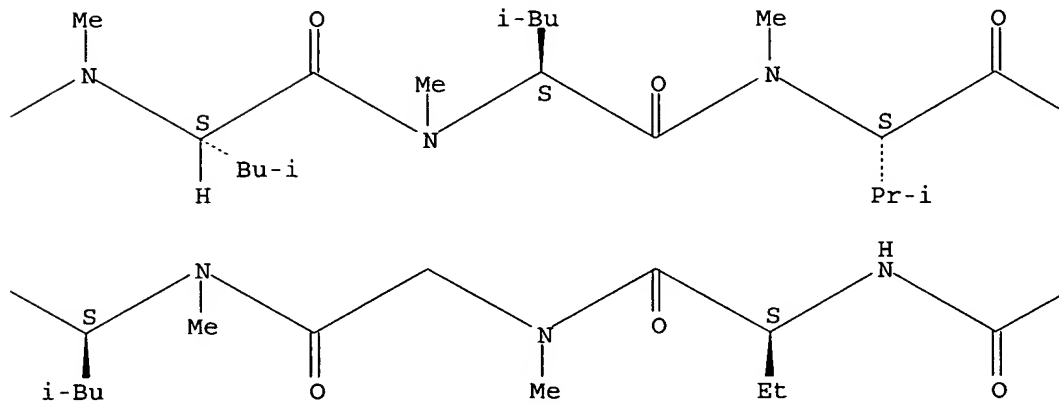
CN Cyclosporin A, 6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

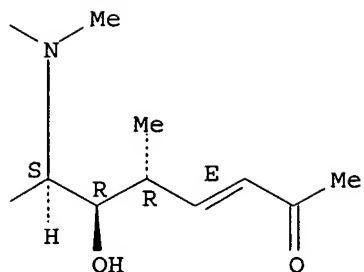
PAGE 1-A



PAGE 1-B



PAGE 1-C



IT 761448-86-6P 761448-87-7P

RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of novel cyclosporins)

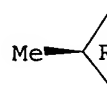
RN 761448-86-6 HCAPLUS

CN Cyclosporin A, 6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]-9-(4-hydroxy-N-methyl-L-leucine)- (9CI) (CA INDEX NAME)

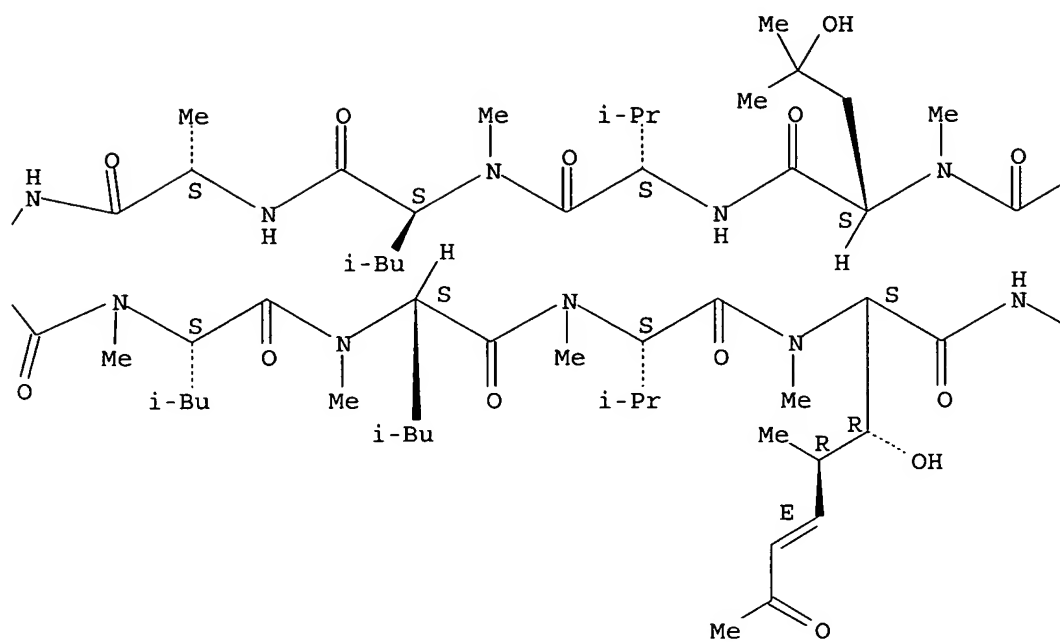
Absolute stereochemistry.

Double bond geometry as shown.

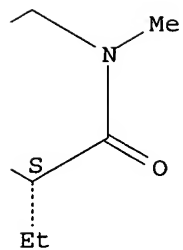
PAGE 1-A



PAGE 1-B

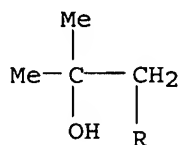
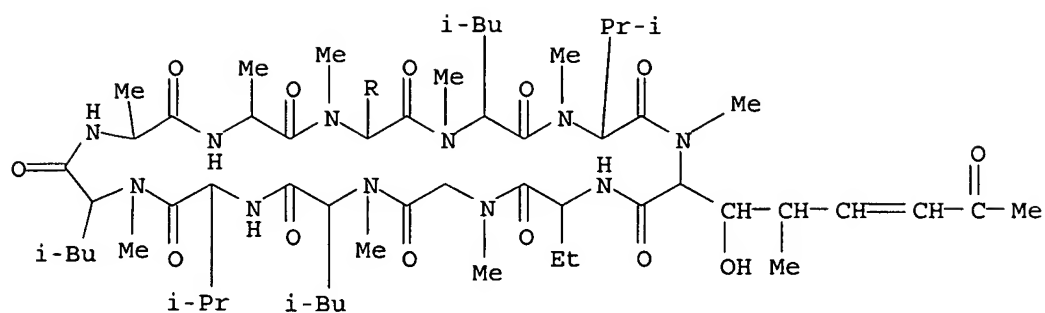


PAGE 1-C



RN 761448-87-7 HCAPLUS  
 CN Cyclosporin A, 3-(4-hydroxy-N-methyl-L-leucine)-6-[(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoic acid]- (9CI) (CA INDEX NAME)





IT 761448-83-3P 761448-84-4P

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

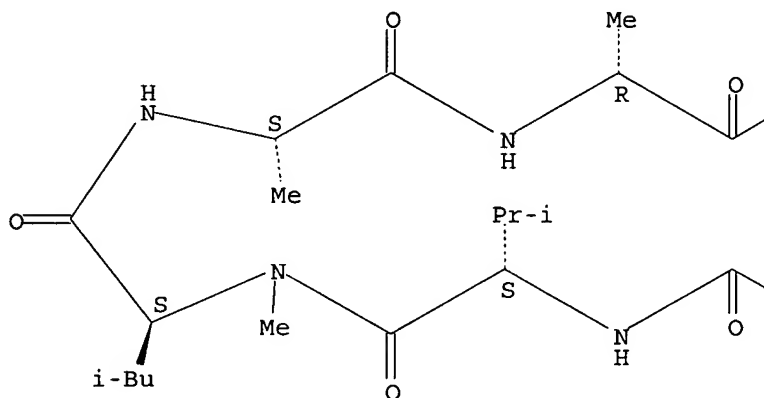
(preparation of novel cyclosporins)

RN 761448-83-3 HCAPLUS

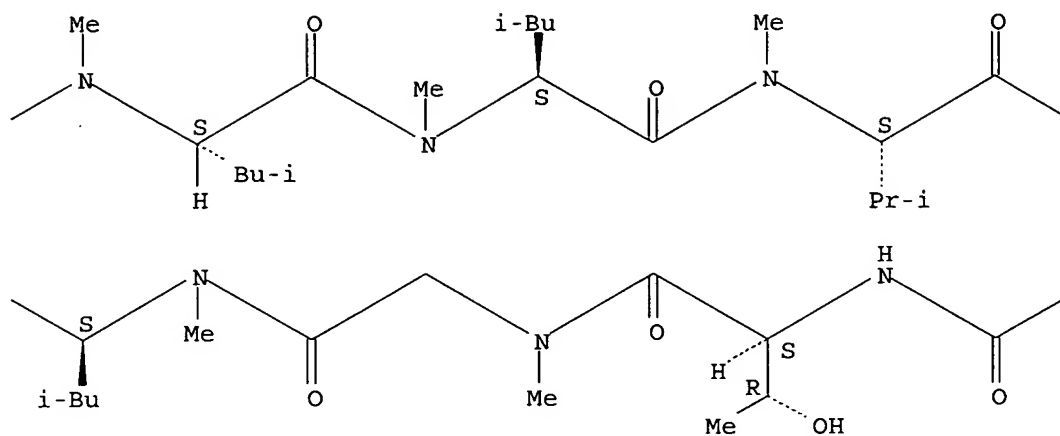
CN Cyclo[L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoyl-L-threonyl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl] (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

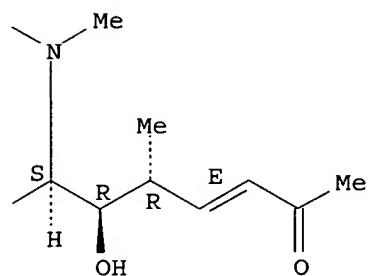
PAGE 1-A



PAGE 1-B



PAGE 1-C

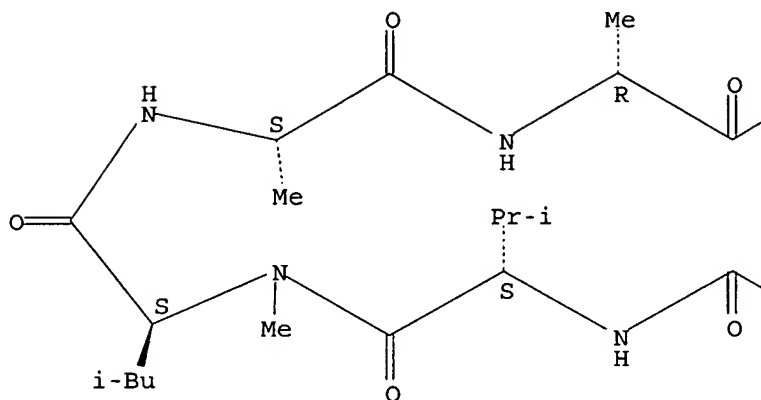


RN 761448-84-4 HCAPLUS

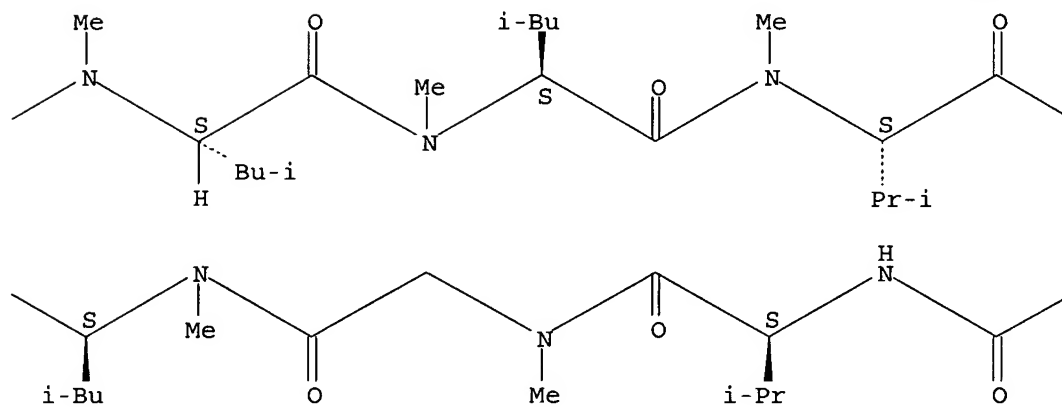
CN Cyclo[L-alanyl-D-alanyl-N-methyl-L-leucyl-N-methyl-L-leucyl-N-methyl-L-valyl-(2S,3R,4R,5E)-3-hydroxy-4-methyl-2-(methylamino)-7-oxo-5-octenoyl-L-valyl-N-methylglycyl-N-methyl-L-leucyl-L-valyl-N-methyl-L-leucyl] (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.  
Double bond geometry as shown.

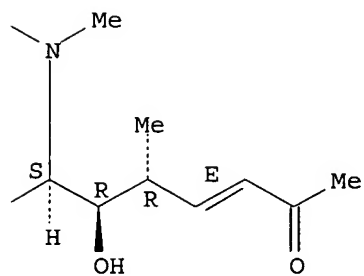
PAGE 1-A



PAGE 1-B

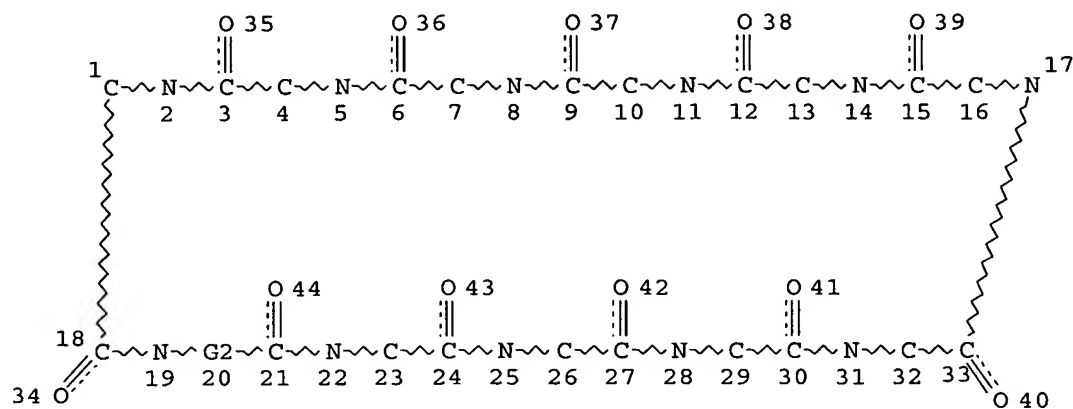


PAGE 1-C



=&gt; =&gt; d stat que

L1 STR



CH $\wedge$ CH3      CH2·CH2·CH2  
 @45 46      @47 48 @49

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

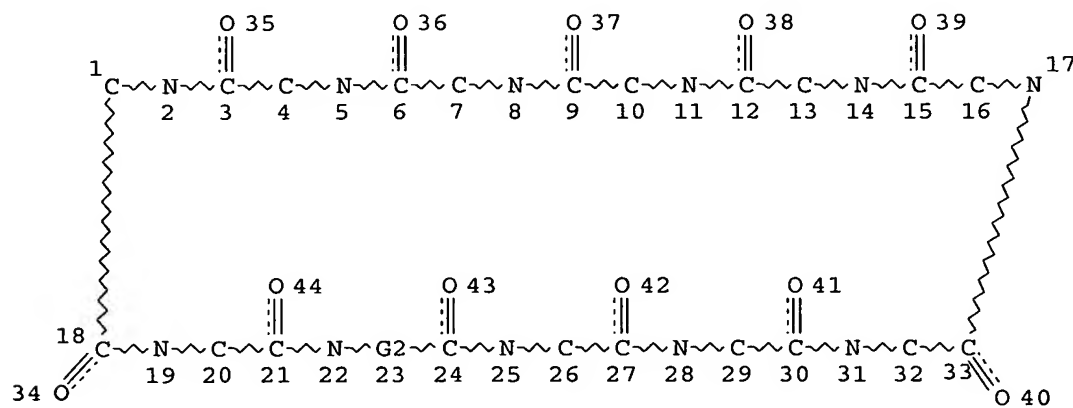
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L2 STR



CH $\wedge$ CH3      CH2·CH2·CH2  
 @45 46      @47 48 @49

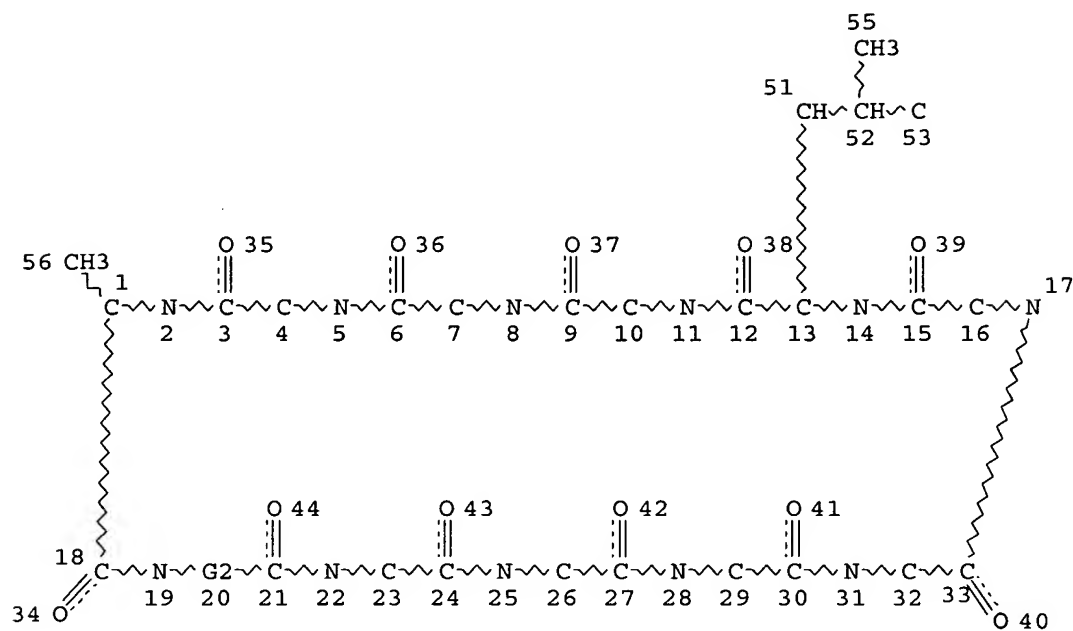
VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE  
L3 1666 SEA FILE=REGISTRY SSS FUL L1 OR L2  
L8 STR

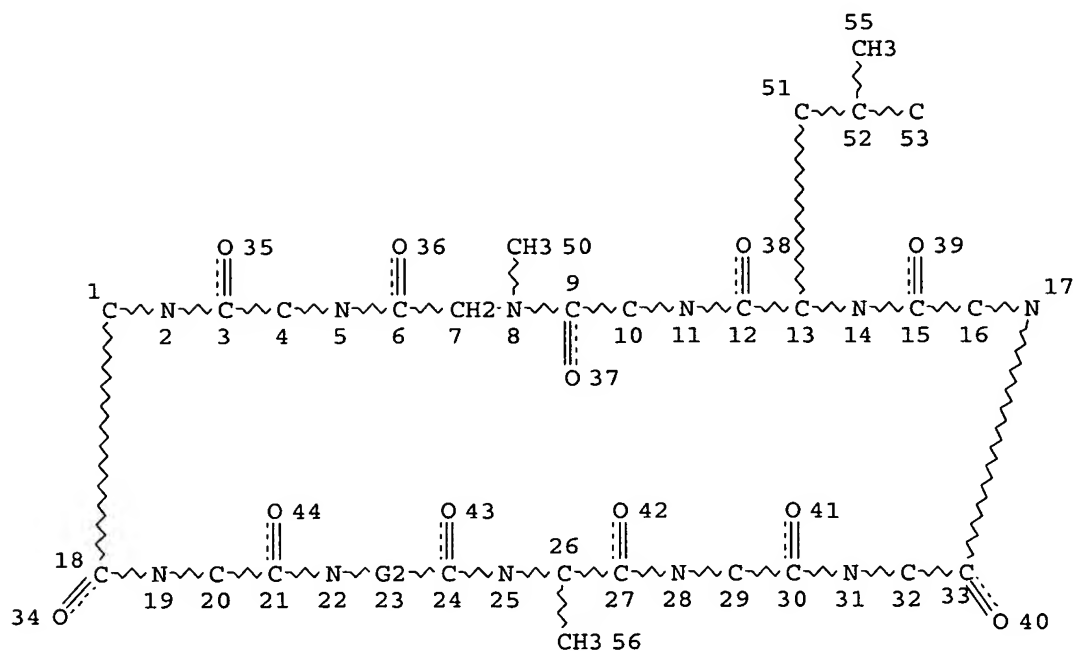


CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

VAR G2=45/47-19 49-21  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE  
L22 STR



CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

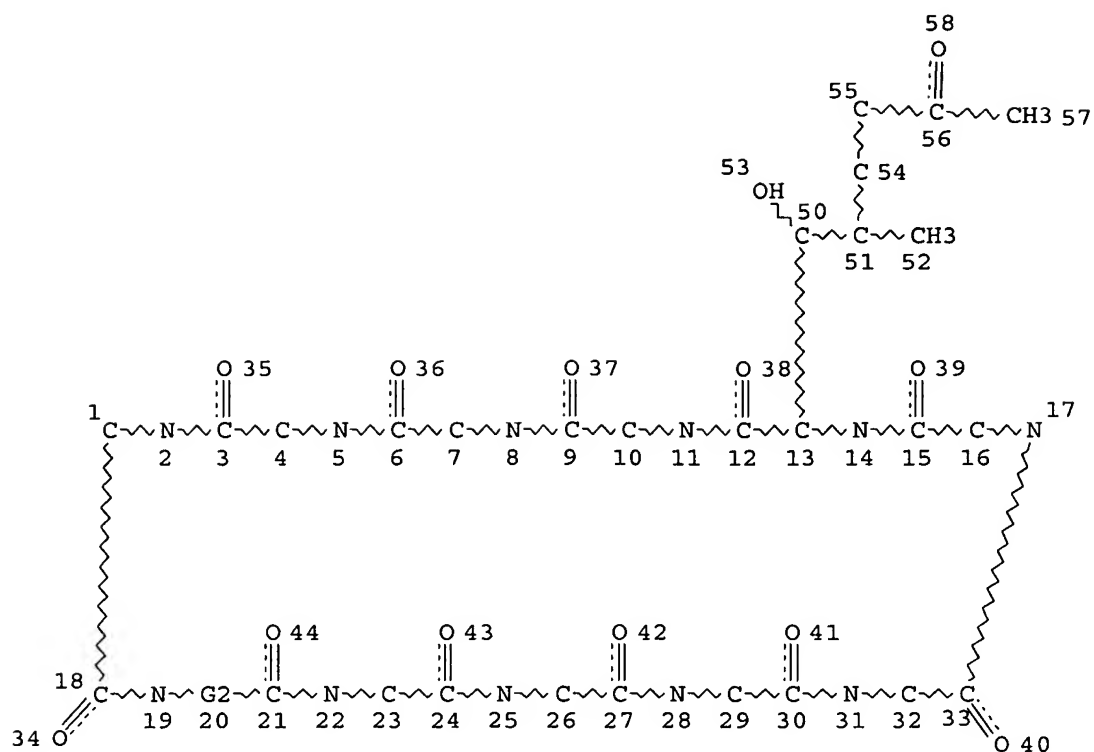
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L23            2 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 AND L22

L27            6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

L28            STR



Page 1-A

CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

Page 2-A

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

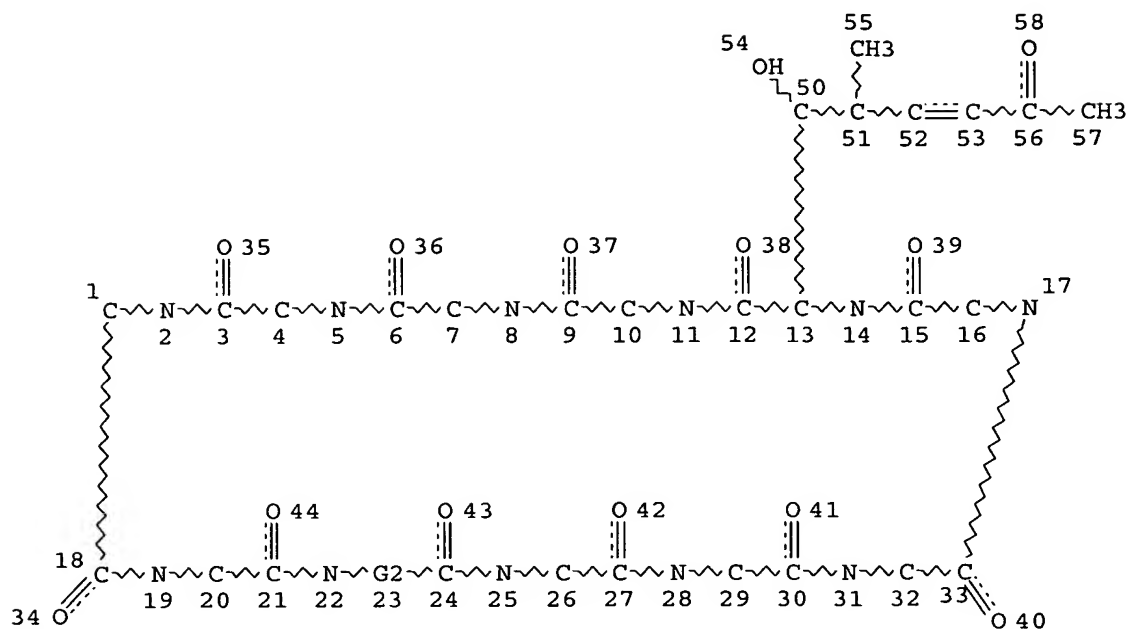
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L29              STR



CH~CH3      CH2-CH2-CH2  
 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

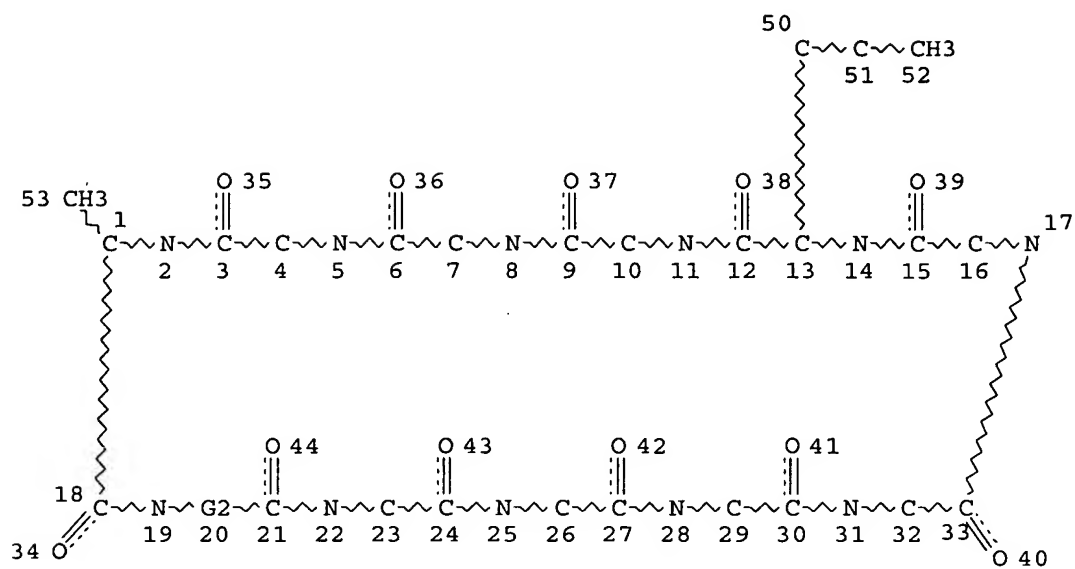
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L30            5 SEA FILE=REGISTRY SUB=L3 SSS FUL L28 OR L29  
 L31            5 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L23  
 L32            1 SEA FILE=HCAPLUS ABB=ON PLU=ON L31  
 L33            1 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L27  
 L39            STR



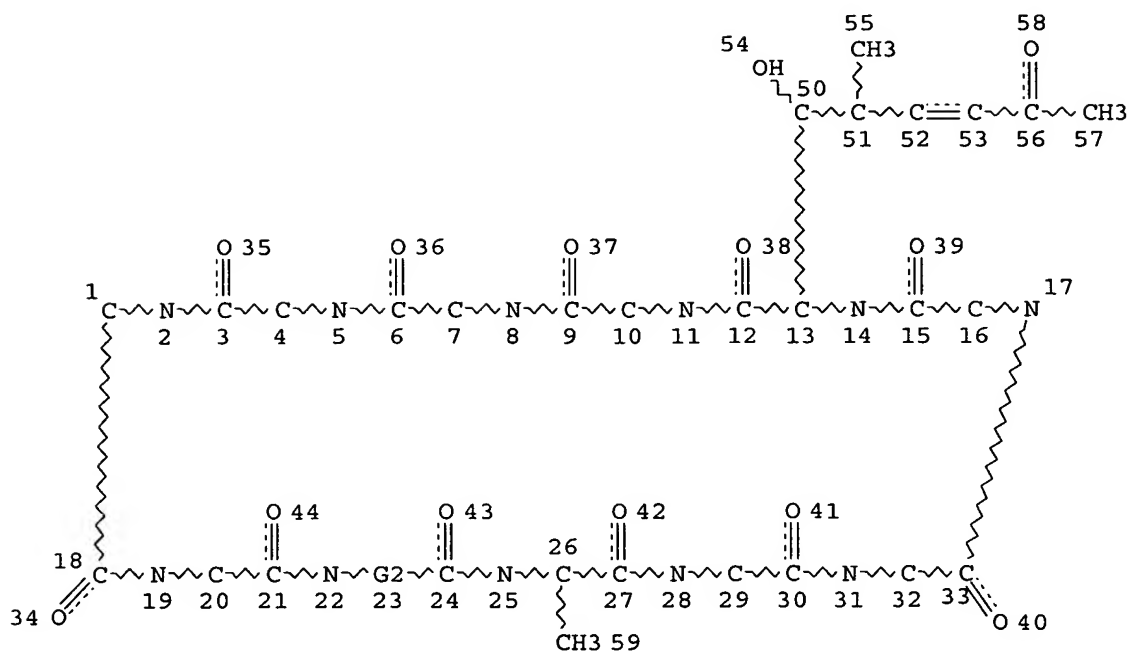


CH~CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

VAR G2=45/47-19 49-21  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 53

STEREO ATTRIBUTES: NONE  
L40                  STR



CH~CH3      CH2-CH2-CH2  
 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 59

STEREO ATTRIBUTES: NONE

L41            15 SEA FILE=REGISTRY SUB=L3 SSS FUL L39 OR L40

L42            8 SEA FILE=REGISTRY ABB=ON PLU=ON L41 NOT (L23 OR L31)

L43            6 SEA FILE=HCAPLUS ABB=ON PLU=ON L42

L44            6 SEA FILE=HCAPLUS ABB=ON PLU=ON L43 NOT (L27 OR L33)

=>

=>

=> d ibib abs hitstr l44 1-6

L44 ANSWER 1 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:888508 HCAPLUS

DOCUMENT NUMBER: 137:389029

TITLE: Use of 3-position cyclosporin derivatives for hair growth

INVENTOR(S): Kim, Sang-Nyun; Ahn, Ho-Jeong; Lee, Chang-Woo; Lee, Min-Ho; Kim, Jung-Hun; Kim, Jong-Il; Kim, Seung-Jin; Cho, Ho-Song; Lee, Heon-Sik; Kim, Hyung-Jin

PATENT ASSIGNEE(S): LG Household & Health Care Ltd., S. Korea  
 SOURCE: PCT Int. Appl., 52 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002092032	A1	20021121	WO 2002-KR879	20020511
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
KR 2002086041	A	20021118	KR 2001-25682	20010511
CA 2446971	AA	20021121	CA 2002-2446971	20020511
EP 1387660	A1	20040211	EP 2002-728237	20020511
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2002009619	A	20040330	BR 2002-9619	20020511
CN 1507339	A	20040623	CN 2002-809675	20020511
TR 200301931	T2	20040921	TR 2003-200301931	20020511
JP 2004530685	T2	20041007	JP 2002-588951	20020511
US 2003207798	A1	20031106	US 2002-303281	20021125
US 6762164	B2	20040713		
ZA 2003008532	A	20040701	ZA 2003-8532	20031031
PRIORITY APPLN. INFO.:				
			KR 2001-25682	A 20010511
			US 2002-141723	A3 20020509
			WO 2002-KR879	W 20020511

OTHER SOURCE(S): MARPAT 137:389029

AB The present invention discloses a hair growth promoting agent comprising a cyclosporin derivative as an active ingredient, and more particularly, a hair growth promoting agent comprising a cyclosporin A derivative substituted in the 3-position as an active ingredient. [N-methyl-D-Abu3]cyclosporin A was prepared by alkylation of cyclosporin A with EtI and the compound formulated in a hair tonic.

IT 475637-01-5P

RL: COS (Cosmetic use); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (use of 3-position cyclosporin derivs. for hair growth)

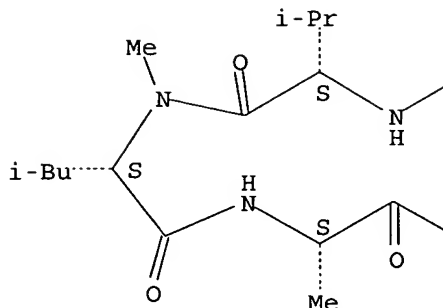
RN 475637-01-5 HCAPLUS

CN Cyclosporin A, 8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)

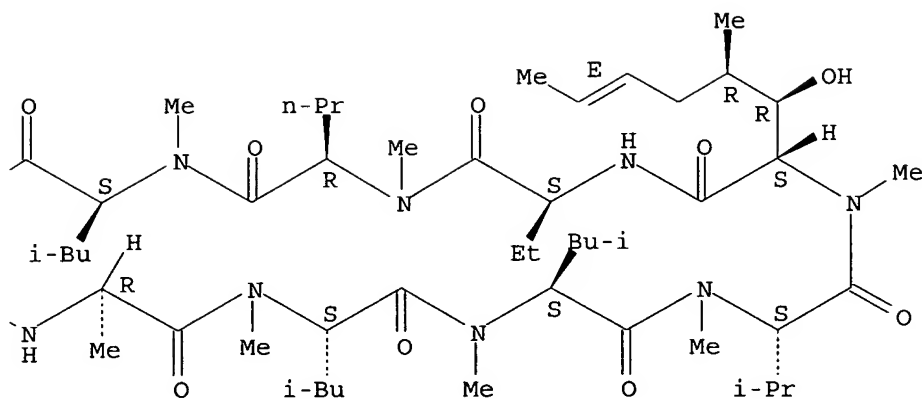
Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:13713 HCAPLUS

DOCUMENT NUMBER: 122:10532

TITLE: Derivatives of a Novel Cyclopeptolide. 2. Synthesis, Activity against Multidrug Resistance in CHO and KB Cells in vitro, and Structure-Activity Relationships

AUTHOR(S): Emmer, Gerhard; Grassberger, Maximilian A.; Schulz, Gerhard; Boesch, Danielle; Gaveriaux, Claire; Loor, Francis

CORPORATE SOURCE: Department of Dermatology, SANDOZ Forschungsinstitut, Vienna, A-1235, Austria

SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 1918-28  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A series of derivs. of the novel antifungal cyclopeptolide  
cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-(R)-

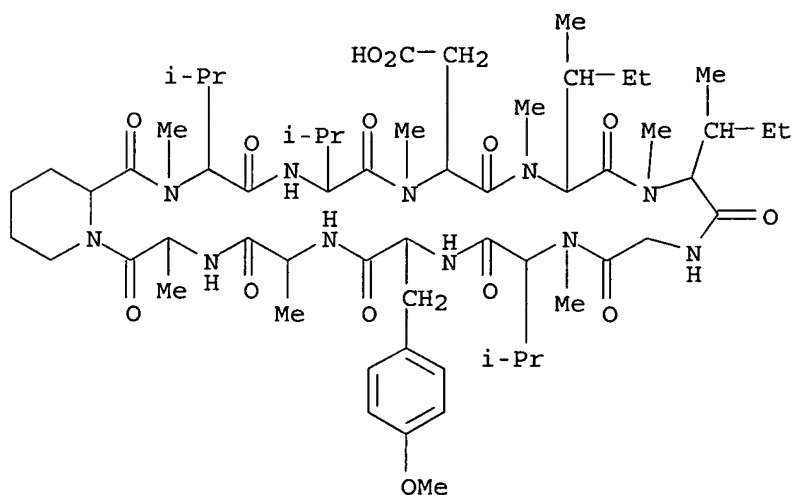
Lac10], (1; Pec = L-pipecolic acid, Lac = lactic acid) was prepared, and their ability to chemosensitize multi drug resistant CHO and KB cells in vitro was evaluated. In contrast to the parent compound, several of the derivs. were highly active. In particular, conversion of the R-lactic acid residue of 1 into its S-isomer via lactone ring cleavage and recyclization with inversion resulted in a marked enhancement of activity. Some of these derivs., e.g. cyclo[Pec-MeVal-Val-MeAsp(OCMe3)-MeIle-MeIle-Gly-MeVal-Tyr(Me)-(S)-Lac] (SDZ 280.446) belong to the most potent resistance modulating compds. known so far.

IT 159105-13-2

RL: RCT (Reactant); RACT (Reactant or reagent)  
(drug resistance modulating activity of)

RN 159105-13-2 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L- $\alpha$ -aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)



L44 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:13712 HCAPLUS

DOCUMENT NUMBER: 122:10531

TITLE: Derivatives of a Novel Cyclopeptolide. 1. Synthesis, Antifungal Activity, and Structure-Activity Relationships

AUTHOR(S): Emmer, Gerhard; Grassberger, Maximilian A.; Meingassner, Josef G.; Schulz, Gerhard; Schauder, Michael

CORPORATE SOURCE: Department of Dermatology, SANDOZ Forschungsinstitut, Vienna, A-1235, Austria

SOURCE: Journal of Medicinal Chemistry (1994), 37(13), 1908-17  
CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The synthesis of a series of derivs. of the novel antifungal cyclopeptolide cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-(R)-Lac10], (1; Pec = L-pipecolic acid, Lac = lactic acid), is described. Besides functional group variation of MeAsp4 (esters, amides, and alc. derivs.) and Tyr(Me)9 derivs., opening of the lactone by LiOH in

THF/H<sub>2</sub>O allowed manipulation of the hydroxy group of (R)-Lac10 in the resulting acyclic peptide 15. Recyclization of 15 under Mitsunobu conditions followed by deprotection led to the (S)-Lac10 analog. Cyclic decapeptides, as well as cyclic undecapeptides, were obtained via corresponding modified linear peptides by cyclization. Methylation of all secondary amide groups by MeI and KH/18-crown-6 gave the permethylated compound Two derivs., cyclo[Pec1-MeVal2-Val3-MeAsp4-MeIle5-MeIle6-Gly7-MeVal8-Tyr(Me)9-X10] [X10 = (S)-Lac, D-Ala], showed superior activities against yeasts in vitro at pH 6.5 as compared to 1, but not at a lower pH (4.5).

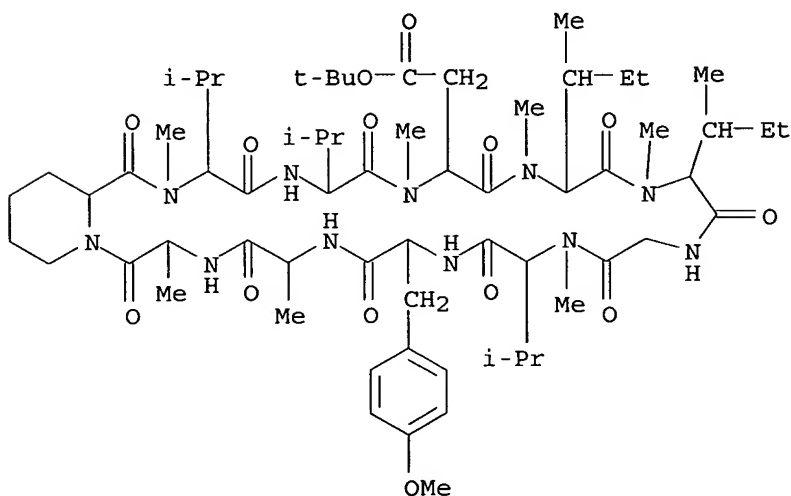
IT 129816-82-6P

RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation, acidic deesterification, and antifungal activity of)

RN 129816-82-6 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-L-methyl-L- $\alpha$ -aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



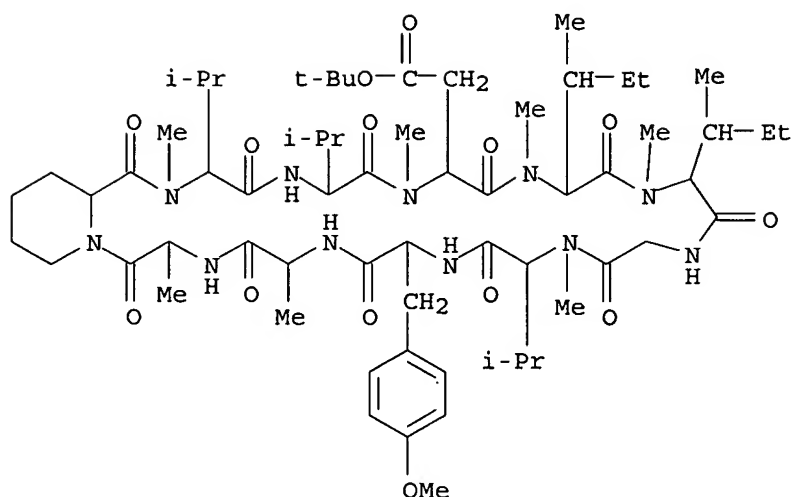
IT 129893-90-9P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and acidic deesterification of)

RN 129893-90-9 HCAPLUS

CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L- $\alpha$ -aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

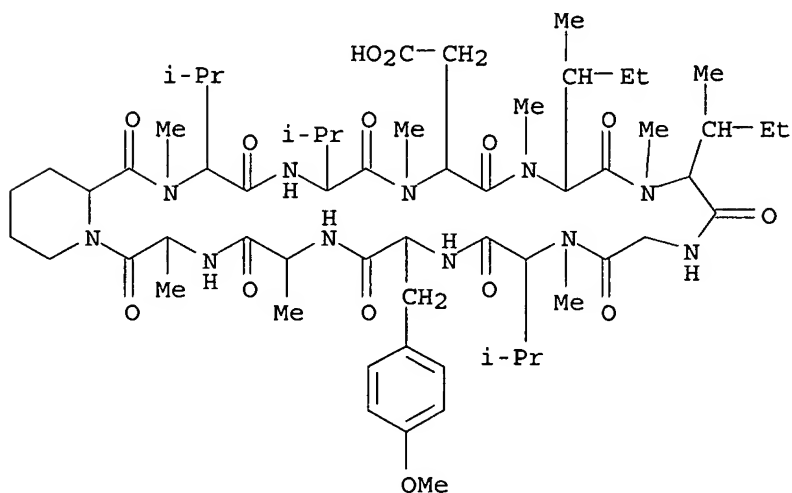


IT 159105-13-2P 159170-93-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and antifungal activity of)

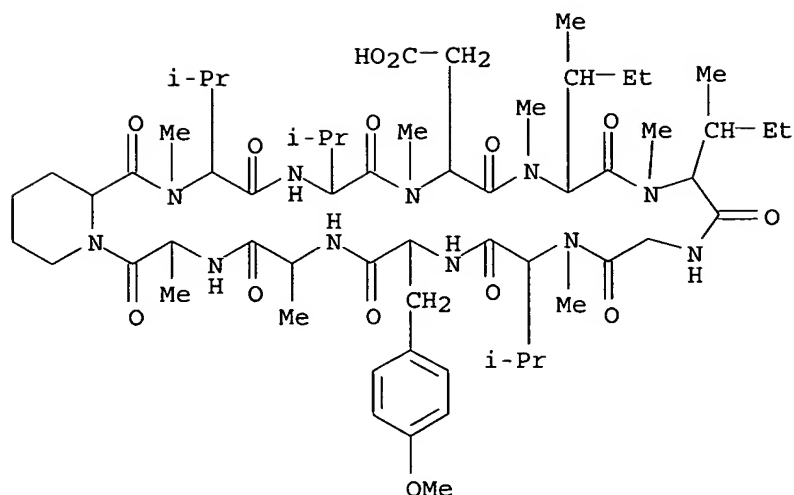
RN 159105-13-2 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)



RN 159170-93-1 HCAPLUS

CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L-α-aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl] (9CI) (CA INDEX NAME)



L44 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:671687 HCAPLUS

DOCUMENT NUMBER: 119:271687

TITLE: Modification of cyclosporin A (CS): generation of an enolate at the sarcosine residue and reactions with electrophiles

AUTHOR(S): Seebach, Dieter; Beck, Albert K.; Bossler, Hans G.; Gerber, Christian; Ko, Soo Y.; Murtiashaw, C. William; Naef, Reto; Shoda, Shinichiro; Thaler, Adrian; et al.

CORPORATE SOURCE: Lab. Org. Chem., Eidg. Techn. Hochsch., Zurich, CH-8092, Switz.

SOURCE: Helvetica Chimica Acta (1993), 76(4), 1564-90

CODEN: HCACAV; ISSN: 0018-019X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 119:271687

AB Strong bases (LDA or BuLi) convert cyclosporin A (CS) to a hexalithio derivative containing a Li alkoxide, four Li azaenolate, and one Li enolate unit.

The Li<sub>6</sub> compound is solubilized in THF by addition of excess LDA or LiCl. Reactions with electrophiles (alkyl halides, aldehydes, chloroformates, CO<sub>2</sub>, disulfides, D<sub>2</sub>O) at low temps. give products containing new side chains at the sarcosine residue of the cyclic undecapeptide in moderate to high yields and, with Re- or Si-selectivities of up to 7:1, depending upon the lithiation conditions. Pure CS derivs. can be isolated by column chromatog. N-alkylations or cleavage of the peptide backbone by carbonyl addition occur only at higher temps. and/or with prolonged reaction times. Very little or no epimerization of stereogenic centers occurs under the conditions employed. Possible reasons for the feasibility of these surprising conversions of CS are discussed. For comparison, [MeAla<sup>3</sup>]CS and [D-MeAla<sup>3</sup>]CS were also prepared by conventional peptide synthesis in solution. Their <sup>1</sup>H and <sup>13</sup>C NMR spectra are compared with those of CS.

IT 108466-56-4P

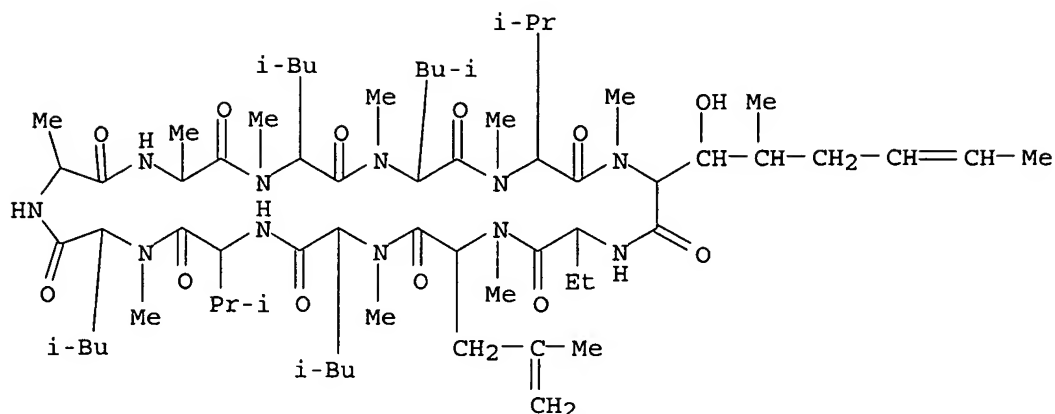
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation of, via stereoselective alkylation of cyclosporin A enolate)

RN 108466-56-4 HCAPLUS

CN Cyclosporin A, 8-(4,5-didehydro-N-methyl-D-leucine)- (9CI) (CA INDEX NAME)





L44 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:572754 HCAPLUS

DOCUMENT NUMBER: 113:172754

TITLE: Manufacture and chemical transformations of cyclopeptolides as medical fungicides and neoplasm inhibitor enhancers

INVENTOR(S): Dreyfuss, Michael M.; Emmer, Gerhard; Grassberger, Maximilian; Rueedi, Klaus; Tschertter, Hans

PATENT ASSIGNEE(S): Sandoz-Patent-G.m.b.H., Germany

SOURCE: Ger. Offen., 44 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

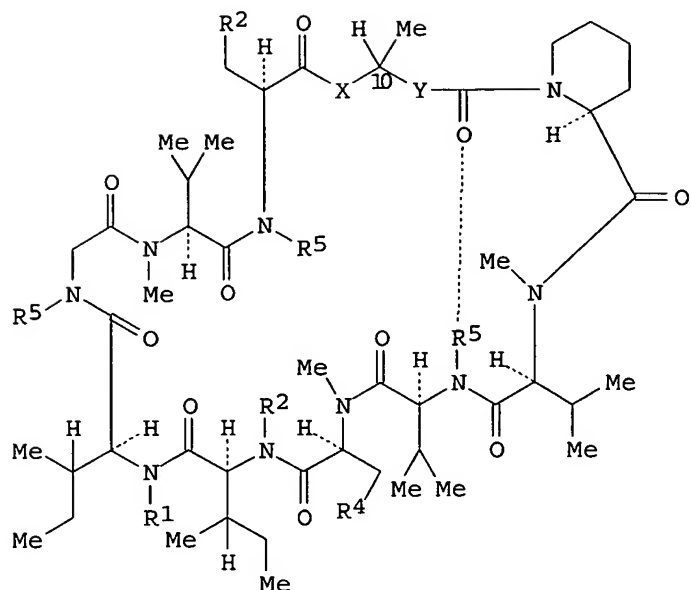
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3832362	A1	19900329	DE 1988-3832362	19880923
HU 51299	A2	19900428	HU 1989-4797	19890908
DK 8904669	A	19900324	DK 1989-4669	19890921
FI 8904480	A	19900324	FI 1989-4480	19890921
EP 360760	A2	19900328	EP 1989-810721	19890921
EP 360760	A3	19901010		
EP 360760	B1	19950215		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
IL 91708	A1	19940530	IL 1989-91708	19890921
ES 2068913	T3	19950501	ES 1989-810721	19890921
CA 1340447	A1	19990316	CA 1989-612370	19890921
AU 8941652	A1	19900405	AU 1989-41652	19890922
AU 628855	B2	19920924		
JP 02134399	A2	19900523	JP 1989-247852	19890922
ZA 8907249	A	19910529	ZA 1989-7249	19890922
US 5643869	A	19970701	US 1995-446983	19950522

PRIORITY APPLN. INFO.:

DE 1988-3832362	A	19880923
US 1989-411336	B1	19890922
US 1992-874277	B1	19920424
US 1994-187929	B1	19940127

OTHER SOURCE(S): CASREACT 113:172754; MARPAT 113:172754

GI



I

AB The title compds. [I; R1, R2, R5 = H, Me; R1, R2 cannot both = H; R3 = R6OC6H4, cyclohexyl, cyclohexenyl, cyclohexadienyl; R4 = COR7, CH2R8, cyano; R6 = H, alkyl, alkenyl, acyl, geranyl, aralkyl, etc.; R7 = H (ar)alkyl, OR9, NR10R11, etc.; R8 = H, halo, alkyl, alkenyl, azido, adamantylcarbonyloxy, naphthylaminocarbonyloxy, etc.; R9 = H, alkyl, alkenyl, aryl, PhCH2, etc.; R10, R11 = H, alkoxy(alkyl), (un)substituted CH2CO2H, furylmethyl, Ph, Ph2CH, etc.; X = O, NH; Y = bond, CONH, CHMe; C-atoms in position 10 have D- or L-config.], specifically I (R3 = 4-MeOC6H4, R4 = CO2H, R5 = H, X = O, Y = bond), were manufactured by harvesting the product of a mycellar suspension of NRRL 15761 and subjecting it to a series of chemical transformations. In vitro, 1.5-25 mg I/mL inhibit fungi, e.g., Candida; in rats, I at 0.1-1% locally gave 100% healing of the intravaginal Candida infection. I enhance the effectiveness of neoplasm inhibitors by restoring the sensitivity of, e.g., carcinoma cells in vivo toward antineoplastic/cyctotoxic drugs.

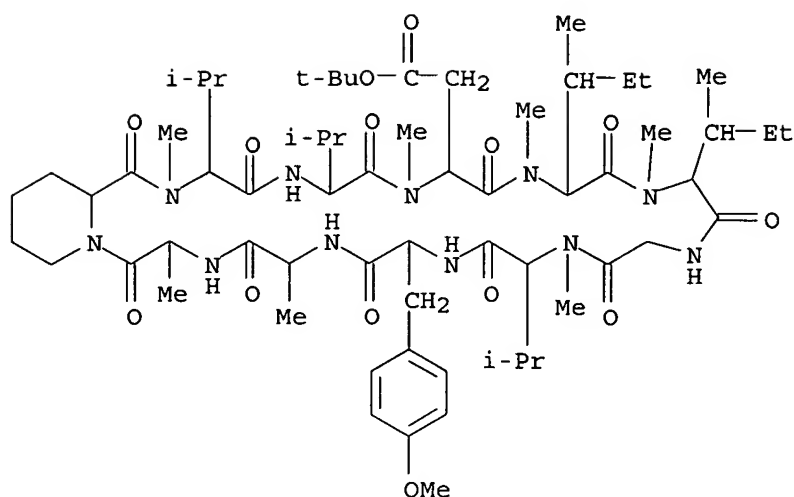
IT 129816-82-6P 129893-90-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

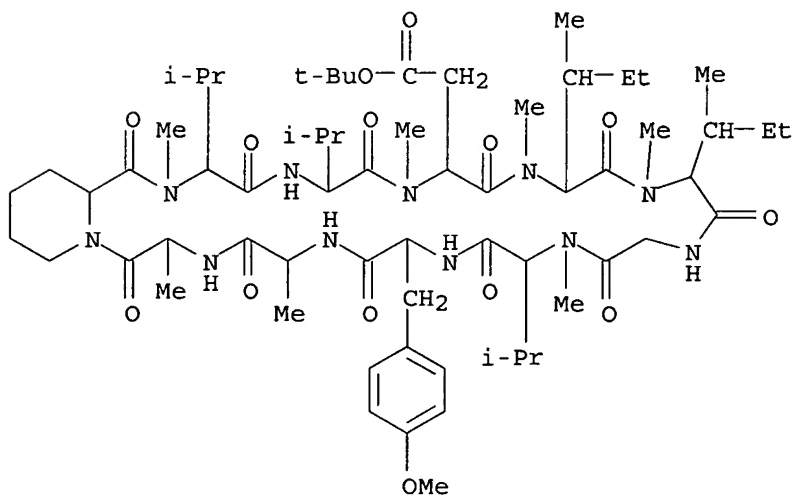
(preparation of, as medical fungicide and neoplasm inhibitor enhancer)

RN 129816-82-6 HCAPLUS

CN Cyclo[D-alanyl-L-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L- $\alpha$ -aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 129893-90-9 HCAPLUS  
 CN Cyclo[D-alanyl-D-alanyl-(2S)-2-piperidinecarbonyl-N-methyl-L-valyl-L-valyl-N-methyl-L- $\alpha$ -aspartyl-N-methyl-L-isoleucyl-N-methyl-L-isoleucylglycyl-N-methyl-L-valyl-O-methyl-L-tyrosyl], 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



L44 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1987:407610 HCAPLUS  
 DOCUMENT NUMBER: 107:7610  
 TITLE: Cyclosporins  
 INVENTOR(S): Seebach, Dieter  
 PATENT ASSIGNEE(S): Sandoz A.-G., Switz.; Sandoz-Patent-G.m.b.H.;  
 Sandoz-Erfindungen Verwaltungsgesellschaft m.b.H.  
 SOURCE: Eur. Pat. Appl., 66 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 194972	A2	19860917	EP 1986-810112	19860306
EP 194972	A3	19890712		
EP 194972	B1	19920729		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 78832	E	19920815	AT 1986-810112	19860306
US 4703033	A	19871027	US 1986-837434	19860307
DK 8601094	A	19860912	DK 1986-1094	19860310
FI 8600993	A	19860912	FI 1986-993	19860310
JP 61212599	A2	19860920	JP 1986-53528	19860310
JP 07059594	B4	19950628		
HU 45272	A2	19880628	HU 1986-1009	19860310
ES 552855	A1	19890116	ES 1986-552855	19860310
ES 552855	A5	19890214		
HU 47137	A2	19890130	HU 1986-1434	19860310
PL 151029	B1	19900731	PL 1986-258350	19860310
PL 151429	B1	19900928	PL 1986-267785	19860310
AU 8654485	A1	19860918	AU 1986-54485	19860311
AU 588860	B2	19890928		
ZA 8601805	A	19871125	ZA 1986-1805	19860311
ES 557619	A1	19880716	ES 1987-557619	19870701
ES 557619	A5	19880816		
US 4771122	A	19880913	US 1987-103990	19871001
AU 8938176	A1	19891102	AU 1989-38176	19890717
PRIORITY APPLN. INFO.:				
			GB 1985-6230	A 19850311
			GB 1985-11029	A 19850501
			GB 1986-2370	A 19860131
			EP 1986-810112	A 19860306
			US 1986-837434	A3 19860307

GI

X-X<sup>1</sup>-X<sup>2</sup>-MeLeu-Val-MeLeu-Ala-D-Ala-MeLeu-MeLeu-MeVal

I

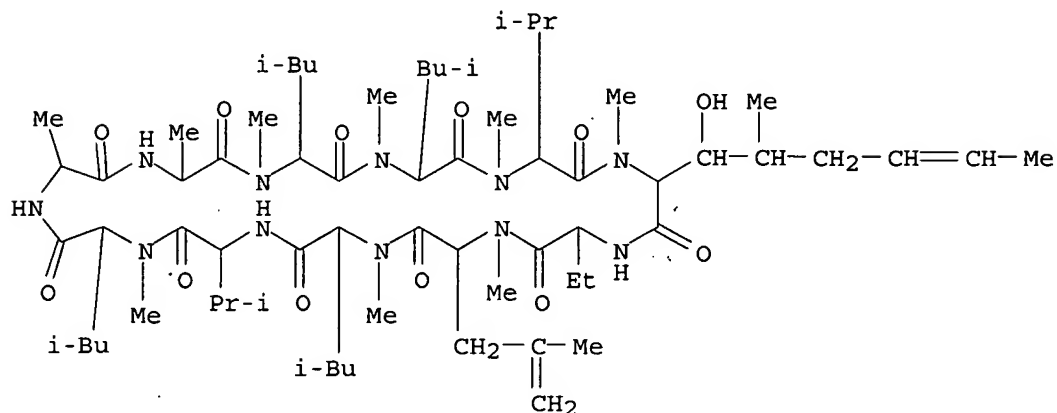
AB The title compds. I [X = (dihydro)-N-methyl-4-[(2E,4R)-but-2-en-1-yl]-4-methyl-L-threonyl (MeBmt); X<sup>1</sup> =  $\alpha$ Abu, Thr, Val, Nva; X<sup>2</sup> = NMeCHRCO; R = halo, cyano, CONH<sub>2</sub>, (un)substituted alkyl, alkylcarbonyl, (un)substituted alkylthio, (un)substituted alkenyl, (hetero)arylthio, etc.], possessing immunosuppressive, antiinflammatory and antiparasitic activity, were prepared by treating cyclosporins with a base and reacting the resulting cyclosporin polyanions having a deprotonated sarcosine residue (I; X<sup>2</sup> = sarcosyl) with electrophiles, e.g. aldehydes, isocyanates, disulfides, alkyl halides. Thus, cyclosporin A in THF was added dropwise to 6.7 equiv (Me<sub>2</sub>CH)<sub>2</sub>NLi in THF at -78° and after 1 h MeI was added at -78°. The mixture was allowed to warm to room temperature to give I (X = MeBmt; X<sup>1</sup> =  $\alpha$ Abu; X<sup>2</sup> = MeAla). The title compds. at 0.01-10  $\mu$ g/mL inhibited concanavalin A stimulated DNA synthesis, cell-proliferation and blasto-genesis in mouse spleen lymphocytes and at 1-30 mg/kg/day p.o. were active against arthritis in rats, and at 10-50 mg/kg/day p.o. doubled the survival time of mice infected with malaria.

IT 108466-56-4P 108466-74-6P 108466-75-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as immunosuppressive, antiinflammatory, and antiparasitic agent)

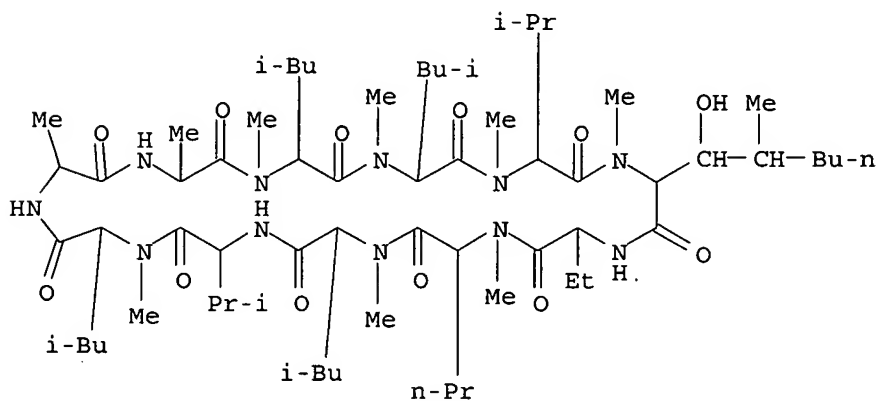
RN 108466-56-4 HCAPLUS

CN Cyclosporin A, 8-(4,5-didehydro-N-methyl-D-leucine)- (9CI) (CA INDEX NAME)



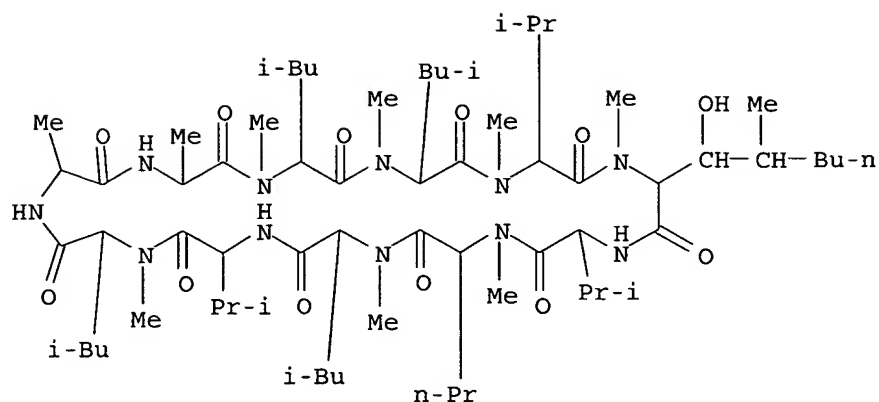
RN 108466-74-6 HCAPLUS

CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)

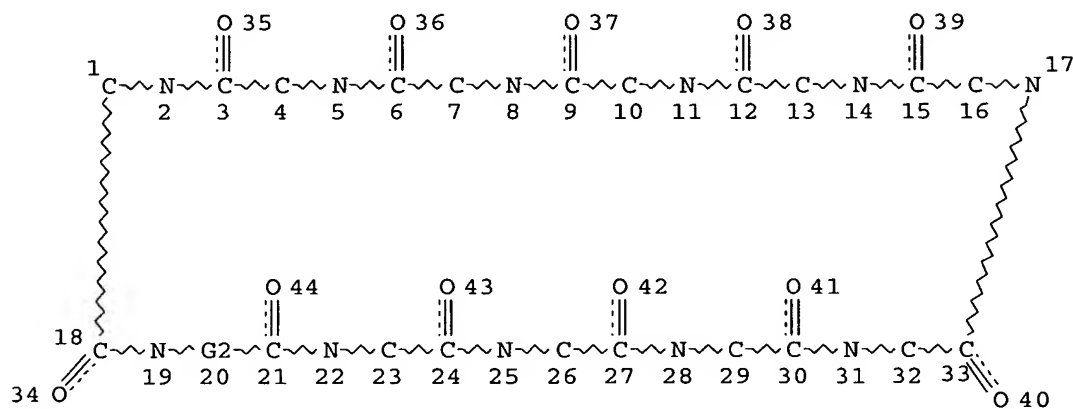


RN 108466-75-7 HCAPLUS

CN Cyclosporin A, 6-[(3R,4R)-3-hydroxy-N,4-dimethyl-L-2-aminooctanoic acid]-7-L-valine-8-(N-methyl-D-norvaline)- (9CI) (CA INDEX NAME)



=> => d stat que 156  
L1 STR

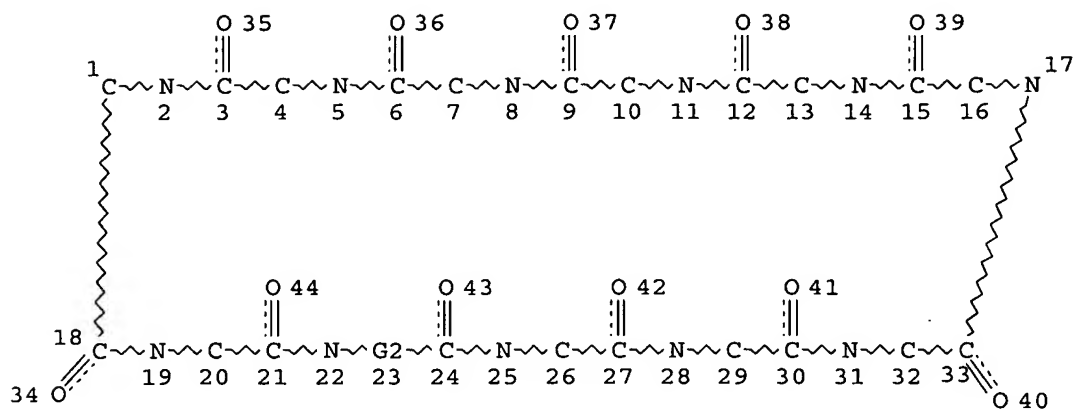


CH<sup>^</sup>CH3      CH2·CH2·CH2  
@45 46      @47 48 @49

VAR G2=45/47-19 49-21  
NODE ATTRIBUTES:  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE  
L2 STR



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@45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

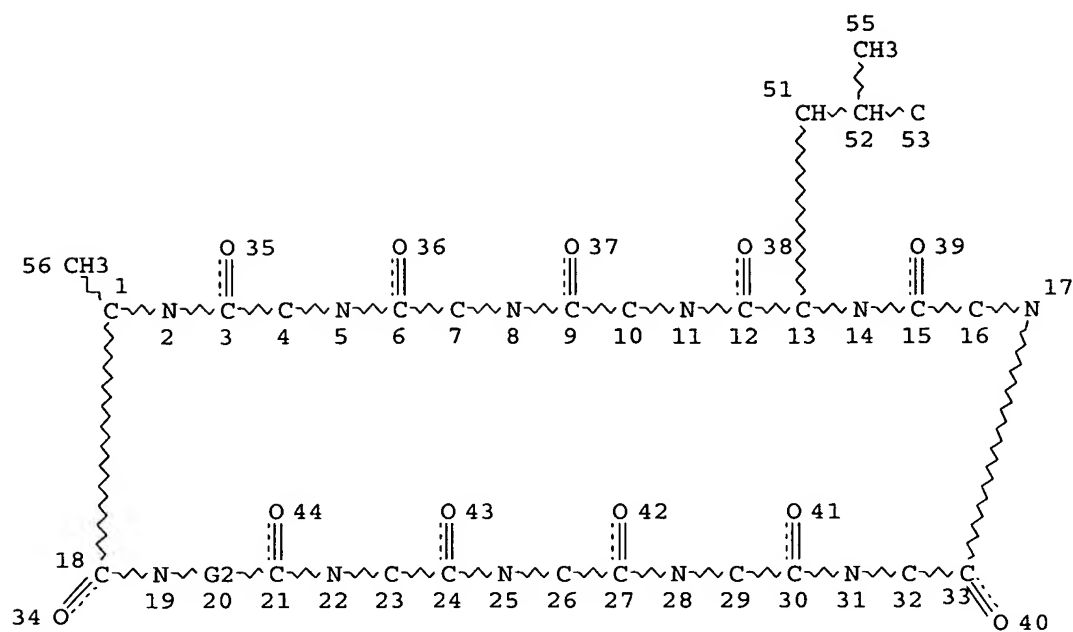
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 49

STEREO ATTRIBUTES: NONE

L3      1666 SEA FILE=REGISTRY SSS FUL L1 OR L2

L8      STR



CH~CH3      CH2-CH2-CH2  
@45 46      @47 48 @49

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

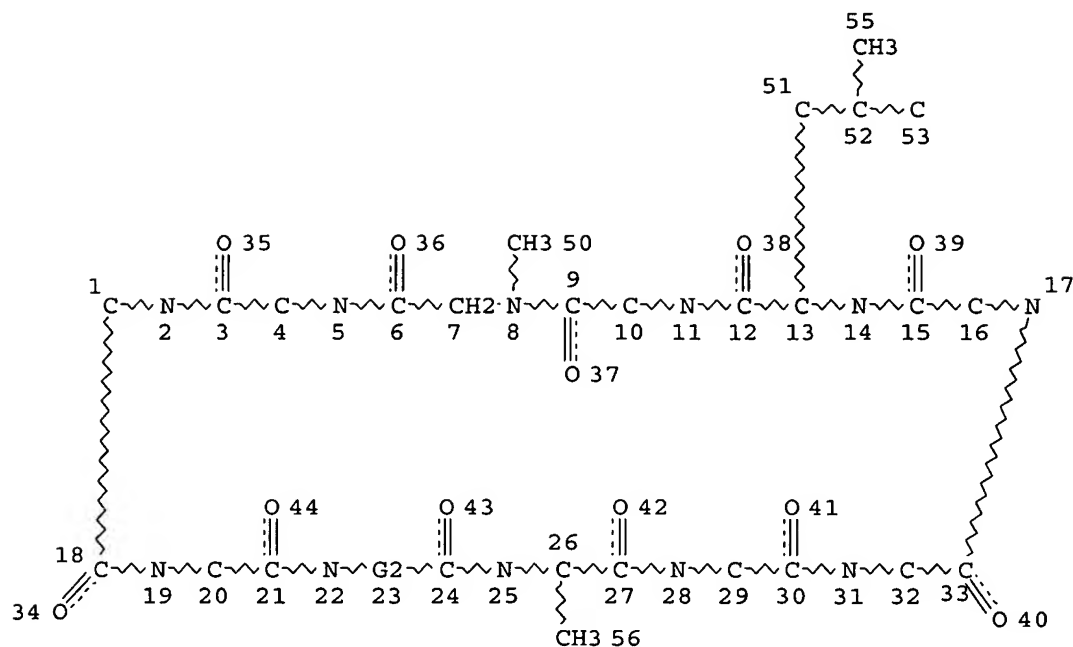
RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 54

STEREO ATTRIBUTES: NONE

L22              STR





CH~CH3      CH2·CH2·CH2  
 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

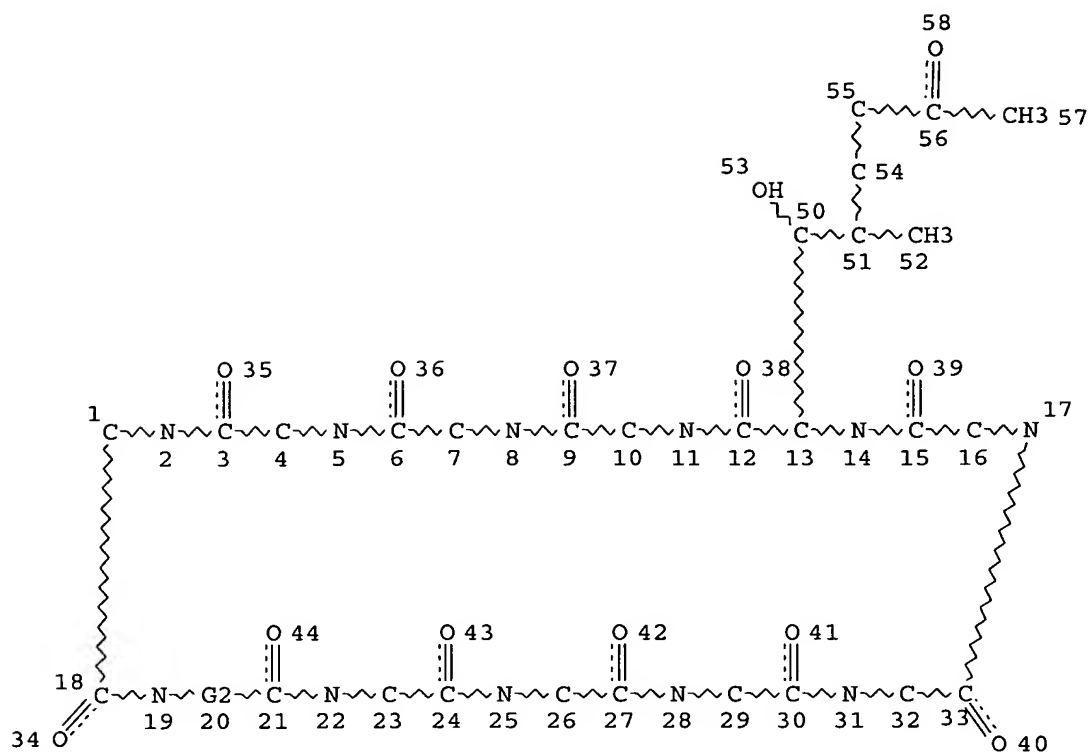
NUMBER OF NODES IS 55

STEREO ATTRIBUTES: NONE

L23            2 SEA FILE=REGISTRY SUB=L3 SSS FUL L8 AND L22

L27            6 SEA FILE=HCAPLUS ABB=ON PLU=ON L23

L28            STR



Page 1-A

CH~CH3      CH2·CH2·CH2  
 @45 46      @47 48 @49

Page 2-A

VAR G2=45/47-19 49-21

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

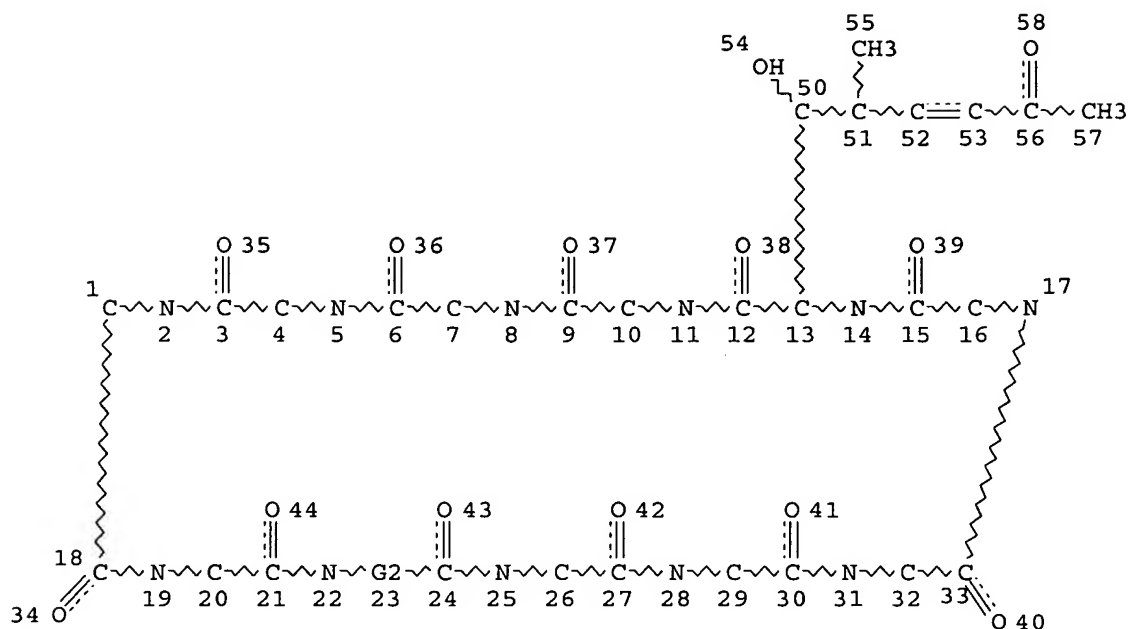
GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L29              STR



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 @45 46      @47 48 @49

VAR G2=45/47-22 49-24

NODE ATTRIBUTES:

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 58

STEREO ATTRIBUTES: NONE

L30      5 SEA FILE=REGISTRY SUB=L3 SSS FUL L28 OR L29  
 L31      5 SEA FILE=REGISTRY ABB=ON PLU=ON L30 NOT L23  
 L32      1 SEA FILE=HCAPLUS ABB=ON PLU=ON L31  
 L33      1 SEA FILE=HCAPLUS ABB=ON PLU=ON L32 NOT L27  
 L45      49 SEA FILE=HCAPLUS ABB=ON PLU=ON "MOLINO B"/AU OR "MOLINO B  
          F"/AU OR ("MOLINO BRUCE"/AU OR "MOLINO BRUCE F"/AU OR "MOLINO  
          BRUCE FRANCIS"/AU)  
 L46      21 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HAYDAR S"/AU OR "HAYDAR S  
          N"/AU) OR "HAYDAR SIMON"/AU OR "HAYDAR SIMON N"/AU  
 L47      9 SEA FILE=HCAPLUS ABB=ON PLU=ON ("HEMENWAY MICHAEL S"/AU OR  
          "HEMENWAY MICHAEL SCOTT"/AU)  
 L49      76 SEA FILE=HCAPLUS ABB=ON PLU=ON L45 OR L46 OR L47  
 L50      563 SEA FILE=HCAPLUS ABB=ON PLU=ON "YANG Z"/AU OR YANG ZHICAI?/AU  
  
 L51      105 SEA FILE=HCAPLUS ABB=ON PLU=ON "RICH JOSEPH"/AU OR ("RICH  
          JOSEPH O"/AU OR "RICH JOSEPH OSWALD"/AU) OR RICH J/AU OR RICH  
          J O/AU  
 L52      1 SEA FILE=HCAPLUS ABB=ON PLU=ON L50 AND L51  
 L54      22554 SEA FILE=HCAPLUS ABB=ON PLU=ON L3 OR ?CYCLOSPOR?

L55 5 SEA FILE=HCAPLUS ABB=ON PLU=ON (L50 OR L51) AND L54  
 L56 77 SEA FILE=HCAPLUS ABB=ON PLU=ON (L49 OR L52 OR L55) NOT (L33  
 OR L27)

=> d ibib abs l56 1-77

L56 ANSWER 1 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:248290 HCAPLUS  
 TITLE: Substituted 3-arylsulfonyl-7-azaindoles as novel 5-HT6  
 agonists  
 AUTHOR(S): McDevitt, Robert E.; Antane, Schuyler A.; Beyer, Chad  
 E.; Chen, Ping; Gross, Jonathan L.; Haydar, Simon  
 N.; Hughes, Zoe. A.; Le, Van-Duc; Mabrouk, Omar;  
 Malberg, Jessica E.; Robichaud, Albert J.; Shenoy,  
 Rajesh A.; Smith, Deborah L.; Wang, Xintao G.; Zhang,  
 Guo Ming; Schechter, Lee. E.  
 CORPORATE SOURCE: Department of Medicinal Chemistry, Chemical and  
 Screening Sciences, Wyeth Research, Princeton, NJ,  
 08543, USA  
 SOURCE: Abstracts of Papers, 231st ACS National Meeting,  
 Atlanta, GA, United States, March 26-30, 2006 (2006),  
 MEDI-137. American Chemical Society: Washington, D.  
 C.  
 CODEN: 69HYEC  
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)  
 LANGUAGE: English  
 AB In recent years much investigation has been focused on higher-order  
 serotonin receptors in the hopes of elucidating their functional roles.  
 5-HT6 receptors are exclusively localized within the CNS and pos. coupled  
 to an adenylate cyclase second messenger system. The ability of 5-HT6  
 receptors to regulate neurotransmitter release has further demonstrated  
 the potential for this receptor in the treatment of a number of disease  
 targets such as cognition, anxiety and depression. Our earlier work  
 identified novel 3-Arylsulfonyl-7-Azaindoles as potent ligands of 5-HT6  
 receptors. Herein we describe the synthesis and effects of substitutions  
 on the 7-Azaindole core. Select examples within this series were revealed  
 to be full 5-HT6 agonists based on cAMP accumulation studies and were  
 shown to be active in a rat behavioral model of anxiety.

L56 ANSWER 2 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2006:248289 HCAPLUS  
 TITLE: 1-(2-Aminoethyl)-3-(arylsulfonyl)-1-H-7-azaindoles as  
 Novel 5-HT6 receptor ligands  
 AUTHOR(S): Haydar, Simon N.; Antane, Schuyler; Ping,  
 Chen; Gross, Jonathan L.; McDevitt, Bob; Le, Van-Duc;  
 Malberg, Jessica; Robichaud, Albert J.; Shenoy, Rajesh  
 A.; Smith, Deborah L.; Zhang, Guo Ming; Schechter, Lee  
 E.  
 CORPORATE SOURCE: Department of Medicinal Chemistry, Chemical and  
 Screening Sciences, Wyeth Research, Princeton, NJ,  
 08543, USA  
 SOURCE: Abstracts of Papers, 231st ACS National Meeting,  
 Atlanta, GA, United States, March 26-30, 2006 (2006),  
 MEDI-136. American Chemical Society: Washington, D.  
 C.  
 CODEN: 69HYEC  
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)  
 LANGUAGE: English  
 AB The 5-HT6 receptor is one of the latest G-protein coupled receptors (GPCR)

to have been identified in the serotonin family. The central nervous system (CNS) localization of the 5-HT<sub>6</sub> receptors and their affinity for CNS drugs have created intense interest in identifying selective 5-HT<sub>6</sub> receptors modulators as tools for studying the receptor and its' potential therapeutic applications. Novel 1-(aminoethyl)-3-(arylsulfonyl)-1-H-7-azaindoles were prepared and several analogs within this class have been identified as high-affinity 5-HT<sub>6</sub> receptor ligands functioning as full agonists. The synthesis and structure activity relationship of this potent class will be discussed.

L56 ANSWER 3 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:167849 HCAPLUS

TITLE: Aryl- and heteroaryl-substituted tetrahydroisoquinolines and their preparation, pharmaceutical compositions and use thereof to block reuptake of norepinephrine, dopamine, and serotonin for the treatment of neurological and psychological disorders

INVENTOR(S): **Molino, Bruce F.**; Liu, Shuang; Berkowitz, Barry A.; Guzzo, Peter R.; Beck, James P.; Cohen, Marlene

PATENT ASSIGNEE(S): Amr Technology, Inc., USA; Bristol-Myers Squibb Company

SOURCE: PCT Int. Appl., 570 pp.

CODEN: PIXXD2

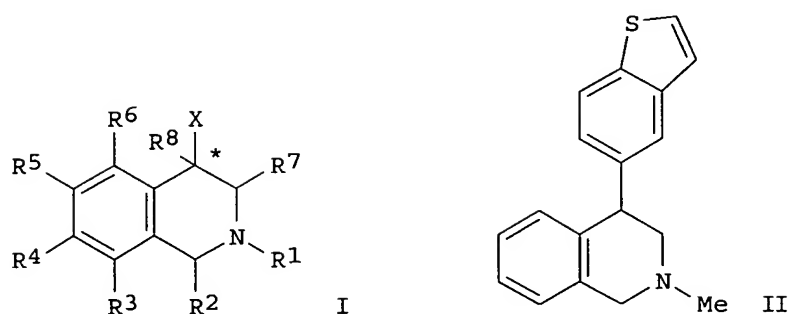
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006020049	A2	20060223	WO 2005-US25193	20050715
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
US 2006052378	A1	20060309	US 2005-183066	20050715
PRIORITY APPLN. INFO.:			US 2004-588448P	P 20040715
GI				



AB This invention discloses the preparation of compds. of formula I and their pharmaceutical composition and use for norepinephrine, dopamine, and serotonin reuptake inhibition to treat neurol. and psychol. disorders and their use in combination therapy. Compds. of formula I wherein \* is in the (R) or (S) configuration; X is (un)substituted fused bicyclic carbocycle or heterocycle; R1 and R7 are independently H, (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cycloalkyl, or (un)substituted C4-7 cycloalkylalkyl; R2 is H, (un)substituted C1-6 (halo)alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cycloalkyl, or (un)substituted C4-7 cycloalkylalkyl; R3, R4, R5, and R6 are independently H, halo, OH and derivs., S(O)NH and derivs., CN, C(O)H and derivs., CONH2 and derivs., NH2 and derivs., (un)substituted C1-6 alkyl, (un)substituted C2-6 alkenyl, (un)substituted C2-6 alkynyl, (un)substituted C3-6 cycloalkyl, or (un)substituted C4-7 cycloalkylalkyl; R8 is H, halo, OH and derivs., SH and derivs., C1-6 alkyl, CN, or NH2 and derivs.; n is 0, 1, or 2; and pharmaceutically acceptable salts and oxides thereof are claimed in this invention. Example compds. (+)- and (-)-II.HCl was prepared by S-alkylation of 4-bromobenzenethiol with bromoacetaldehyde di-Et acetal and the resulting (4-bromophenylsulfanyl)acetaldehyde di-Et acetal underwent cyclization to give 5-bromobenzothiophene that underwent Suzuki coupling with 4-isoquinolinyboronic acid to give 4-(5-benzothiophenyl)isoquinoline, which was N-methylated and the resulting methylated isoquinoline underwent reduction to give tetrahydroisoquinoline derivative that was separated by chiral HPLC to give optically enriched (+)- and

(-)-II, which was treated with HCl to give (+)- and (-)-II.HCl. Addnl. 153 example compds. were prepared using similar procedures. All the invention compds. were evaluated for their ability to block reuptake of norepinephrine, dopamine and serotonin. The functional ability of the invention compds. to inhibit neurotransmitter uptake was established by measuring the inhibition of [3H]-noradrenaline, [3H]-serotonin, and [3H]-dopamine uptake into the rat brain synaptosomes. From the inhibition of radioligand binding at the human biogenic amine transporter assays. it was determined that the invention compds. are potent inhibitors of monoamine reuptake by the dopamine (DAT) norepinephrine (NET) and serotonin (SET) transporters. Compound (+)-II.HCl showed binding affinities (Ki values) of 1.2%, 3.8%, 4.0% inhibition of NET, DAT and SERT resp. at 100 nM concentration

L56 ANSWER 4 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:120480 HCAPLUS

DOCUMENT NUMBER: 144:192506

TITLE: Novel processes for stereoselective synthesis of trans ISATX247

INVENTOR(S): Molino, Bruce F.; Yang, Zhicai;

Maeng, Jun-Ho; Manning, David D.  
 PATENT ASSIGNEE(S): Amr Technology, Inc., USA  
 SOURCE: PCT Int. Appl., 40 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006014872	A2	20060209	WO 2005-US26319	20050726
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			

PRIORITY APPLN. INFO.: US 2004-592330P P 20040729  
 AB The invention relates to a process for preparation of trans ISATX247 and deuterated derivs. cyclo(A-Abu-Sar-MeLeu-Val-MeLeu-Ala-D-Ala-MeLeu-MeLeu-MeVal) [A = -NMeCH[CH(OH)CHMeCH2CH:CHCR3:CR1R2]CO-; stereo  $\alpha$ S, $\beta$ R, $\gamma$ R,E] (R1, R2, R3 = H or D) by application of organozirconium chemical. The process involves reacting an acetyl **cyclosporin** aldehyde with an organozirconium reagent to provide acetyl **cyclosporin** diene (the acetate of trans ISATX247) and deacetylating the acetyl **cyclosporin** diene to produce the trans-isomer of ISATX247. The invention also relates to a process for preparing the same trans ISATX247 compound by olefin cross metathesis of acetyl **cyclosporin** A to afford acetyl **cyclosporin**  $\alpha,\beta$ -unsatd. aldehyde, followed by Wittig reaction and deacetylation. Also disclosed are processes for preparing an acetyl **cyclosporin**  $\alpha,\beta$ -unsatd. aldehyde compound and a **cyclosporin** triene analog compound. Thus, trans ISATX247 acetate was prepared in 47% yield by treating acetyl **cyclosporin** aldehyde with propargyltrimethylsilane, Cp2Zr(H)Cl, and AgClO4 in CH2Cl2.

L56 ANSWER 5 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2005:739631 HCAPLUS  
 TITLE: 1-(2-Aminoethyl)-3-(arylsulfonyl)-1H-pyrrolopyridines as novel 5-HT6 receptor ligands  
 AUTHOR(S): Bernotas, Ronald C.; Antane, Schuyler A.; Lenicek, Steven; Haydar, Simon N.; Robichaud, Albert J.; Zhang, Guo Ming; Smith, Deborah L.; Coupet, Joseph; Schechter, Lee E.  
 CORPORATE SOURCE: Chemical and Screening Sciences, Wyeth Research, Collegeville, PA, 19426, USA  
 SOURCE: Abstracts of Papers, 230th ACS National Meeting, Washington, DC, United States, Aug. 28-Sept. 1, 2005 (2005), MEDI-117. American Chemical Society: Washington, D. C.  
 CODEN: 69HFCL  
 DOCUMENT TYPE: Conference; Meeting Abstract; (computer optical disk)  
 LANGUAGE: English

AB We have demonstrated that many 1-(2-aminoethyl)-3-arylsulfonyl-1H-indoles 2 are 5-HT6 ligands. Introduction of an addnl. nitrogen in the indole ring provided 1-(2-aminoethyl)-3-arylsulfonyl-1H-pyrrolo[1,2,3-b]pyridines 3, which proved to have generally higher 5-HT6 affinity compared to 2. Appropriate substitution on 3 led to full agonists or full antagonists in a 5-HT6 functional (cyclase) assay. We report here the synthesis of the three regioisomeric pyrrolopyridines (4, 5, and 6) by several routes and describe their 5-HT6 binding and functional activity.

L56 ANSWER 6 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:177896 HCAPLUS

DOCUMENT NUMBER: 142:280225

TITLE: Preparation of capped aminopyrazinoylguanidines as sodium channel blockers

INVENTOR(S): Johnson, Michael R.; Molino, Bruce F.; Zhang, Jianzhong; Sargent, Bruce J.

PATENT ASSIGNEE(S): Parion Sciences, Inc., USA

SOURCE: PCT Int. Appl., 100 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005018644	A1	20050303	WO 2004-US26885	20040818
WO 2005018644	B1	20050512		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

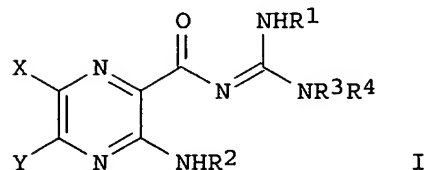
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005080091	A1	20050414	US 2004-920410	20040818
US 2005234072	A1	20051020	US 2005-131262	20050518
US 2005228182	A1	20051013	US 2005-138280	20050527
US 2006052394	A1	20060309	US 2005-211422	20050826
US 2006052395	A1	20060309	US 2005-211660	20050826

PRIORITY APPLN. INFO.: US 2003-495725P P 20030818  
US 2004-920410 A1 20040818

OTHER SOURCE(S): MARPAT 142:280225

GI



AB Title compds. [I; X = H, halo, CF3, alkyl, (substituted) Ph, etc.; Y = H,



OH, SH, alkoxy, alkylthio, halo, alkyl, (substituted) aryl, etc.; R1 = H, alkyl; R2 = R7, (CH<sub>2</sub>)<sub>m</sub>OR8, (CH<sub>2</sub>)<sub>m</sub>NR7R10, (CH<sub>2</sub>CH<sub>2</sub>O)<sub>m</sub>R8, etc.; m = 1-7; R3, R4 = H, alkyl, hydroxyalkyl, Ph, phenylalkyl, naphthylalkyl, pyridylalkyl, etc.; R7 = H, alkyl, (substituted) Ph, etc.; R8 = H, alkyl, 2-tetrahydropyranyl, glucuronide, etc.; R10 = H, SO<sub>2</sub>Me, COR13, CO<sub>2</sub>R13, etc.; R13 = H, R7, R10, etc.; with provisos], were prepared Thus, [4-(4-hydroxyphenyl)butyl]carbamic acid benzyl ester in EtOH at 70° was treated with oxiranylmethanol over 4 h to give 4.6% [4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]carbamic acid benzyl ester. This was hydrogenolyzed in EtOH over Pd/C to give 51% 3-[3-[4-(4-aminobutyl)phenoxy]-2-hydroxypropoxy]propane-1,2-diol. The latter was stirred with Et<sub>3</sub>N and 1-(3,5-diamino-6-chloropyrazine-2-carbonyl)-2-methylisothiourea hydroiodide in EtOH at 65° to give 36% N-(3,5-diamino-6-chloropyrazine-2-carbonyl)-N'-[4-[4-[3-(2,3-dihydroxypropoxy)-2-hydroxypropoxy]phenyl]butyl]guanidine (PSA 15143). The latter showed Na channel blocking activity with EC<sub>50</sub> = 7 nM.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 7 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:934323 HCAPLUS

DOCUMENT NUMBER: 141:395708

TITLE: Substituted heterocycle fused gamma-carbolines

INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael G.; **Haydar, Simon**; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J.; Zawrotny, David M.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 150 pp., Cont.-in-part of U.S. Ser. No. 370,878.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

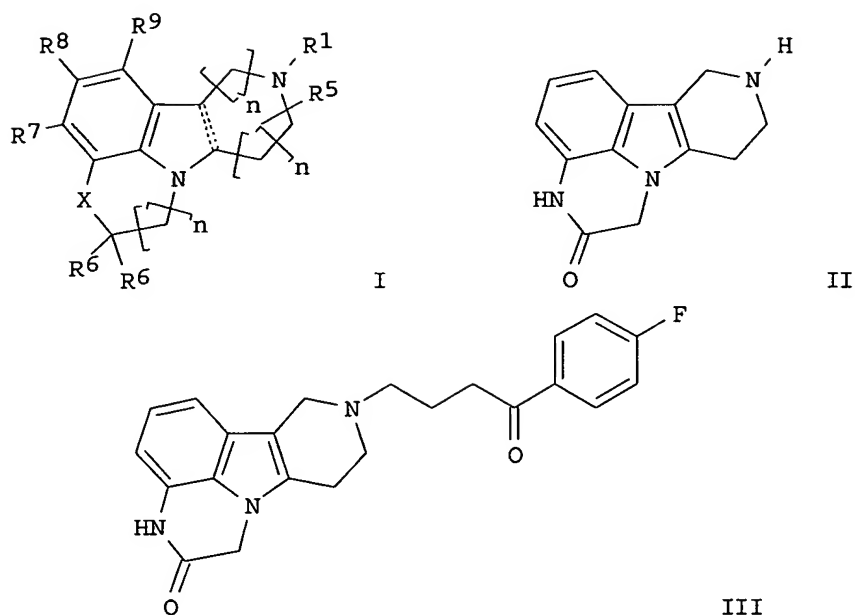
FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 2004220178	A1	20041104	US 2004-787941	20040226
US 6552017	B1	20030422	US 2000-595250	20000615
US 2004034015	A1	20040219	US 2003-370878	20030220
PRIORITY APPLN. INFO.:			US 1999-139321P	P 19990615
			US 2000-595250	A3 20000615
			US 2003-370878	B2 20030220

OTHER SOURCE(S): MARPAT 141:395708

GI



AB The preparation of compds., I ( R 1 = H, ketone, ester, alkyl, alkene, cycloalkyl, aryl; R 5 = H, C1-4 alkyl; R 6 = H, OH, alkylamine, CF<sub>3</sub>, C1-4 alkyl, C2-4 alkenyl, C2-4 alkynyl. C1-4 alkoxy, C1-4 haloalkyl, C3-6 cycloalkyl, aryl; R 7, R 8, R 9 = H, halo, CF<sub>3</sub>, OCF<sub>3</sub>, OH, CN, NO<sub>2</sub>, amine, alkyl, alkenyl etc.; X = NH or substituted amine; dashed line = single or double bond ; n = independently integers form 0-3) as serotonin 5-HT<sub>2</sub> agonists and antagonist for the treatment of addictive behavior and sleep disorders is described. Thus, II was dissolved in Me Et ketone and treated with KI, K<sub>2</sub>CO<sub>3</sub>, and 4-chloro-4'-fluorobutyrophenone to give the target compound III.

L56 ANSWER 8 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:757872 HCAPLUS

DOCUMENT NUMBER: 139:276893

TITLE: Preparation of azabenzothiopyranoindazoles with antitumor activity

INVENTOR(S): Haydar, Simon N.

PATENT ASSIGNEE(S): Albany Molecular Research, Inc., USA

SOURCE: PCT Int. Appl., 73 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

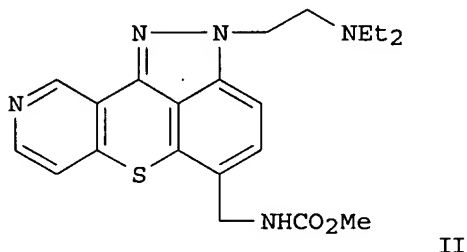
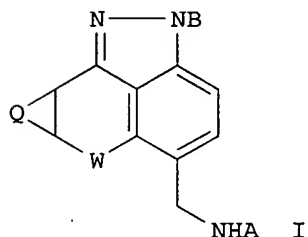
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078647	A2	20030925	WO 2003-US7582	20030311
WO 2003078647	A3	20040408		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,

TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
 KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,  
 FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 US 2003225069 A1 20031204 US 2002-96421 20020312  
 US 6747039 B2 20040608  
 PRIORITY APPLN. INFO.: US 2002-96421 A 20020312  
 OTHER SOURCE(S): MARPAT 139:276893  
 GI



AB Title compds. [I; W = S, SO, SO<sub>2</sub>; Q = 5- or 6-membered aromatic ring having ≥1 N, S; A = H, (substituted) (cyclic) alkyl, alkoxy, OH, CHO, CO<sub>2</sub>R<sub>1</sub>, SO<sub>2</sub>R<sub>1</sub>, (CH<sub>2</sub>)<sub>n</sub>NH(CH<sub>2</sub>)<sub>m</sub>Me, (CH<sub>2</sub>)<sub>n</sub>N[(CH<sub>2</sub>)<sub>m</sub>Me](CH<sub>2</sub>)<sub>p</sub>Me, (CH<sub>2</sub>)<sub>n</sub>D; B = H, (substituted) (cyclic) alkyl, alkoxy, OH, (CH<sub>2</sub>)<sub>n</sub>NH(CH<sub>2</sub>)<sub>m</sub>Me; (CH<sub>2</sub>)<sub>n</sub>N[(CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub>](CH<sub>2</sub>)<sub>p</sub>Me, (CH<sub>2</sub>)<sub>n</sub>D; R<sub>1</sub> = alkyl, Ph, phenylalkyl; n = 2-3; m, p = 0-3; D = OH, (substituted) alkoxy, 5-6 membered (aromatic) heterocyclyl containing S, O, or N], were prepared Thus, title compound (II) (multistep preparation from 3-chlorothiophenol, 4-chloronicotinic acid, and H<sub>2</sub>NNHCH<sub>2</sub>CH<sub>2</sub>NET<sub>2</sub> given) showed GI<sub>50</sub> = 0.1 μM against HeLa S-3 cells.

L56 ANSWER 9 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:757871 HCAPLUS

DOCUMENT NUMBER: 139:276881

TITLE: Preparation of azathioxanthenones with antitumor activity

INVENTOR(S): Haydar, Simon N.

PATENT ASSIGNEE(S): Albany Molecular Research, Inc., USA

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

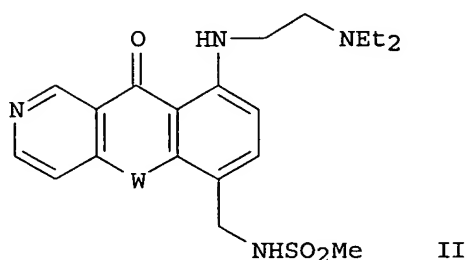
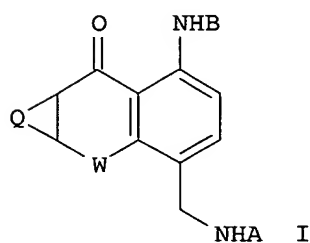
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003078646	A2	20030925	WO 2003-US7581	20030311
WO 2003078646	A3	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,  
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 US 2003212061 A1 20031113 US 2002-96420 20020312  
 PRIORITY APPLN. INFO.: US 2002-96420 A 20020312  
 OTHER SOURCE(S): MARPAT 139:276881  
 GI



AB Title compds. [I; W = S, SO, and SO<sub>2</sub>; Q = atoms to form a 5- or 6-membered aromatic ring having  $\geq 1$  N, S; A = H, (cyclic) (substituted) alkyl, alkoxy, OH, CHO, CO<sub>2</sub>R<sub>1</sub>, SO<sub>2</sub>R<sub>1</sub>, (CH<sub>2</sub>)<sub>n</sub>NH(CH<sub>2</sub>)<sub>m</sub>Me, (CH<sub>2</sub>)<sub>n</sub>N[(CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub>](CH<sub>2</sub>)<sub>p</sub>Me, (CH<sub>2</sub>)<sub>n</sub>D; B = H, (cyclic) (substituted) alkyl, alkoxy, OH, (CH<sub>2</sub>)<sub>n</sub>NH(CH<sub>2</sub>)<sub>m</sub>Me, (CH<sub>2</sub>)<sub>n</sub>N[(CH<sub>2</sub>)<sub>m</sub>CH<sub>3</sub>](CH<sub>2</sub>)<sub>p</sub>Me, (CH<sub>2</sub>)<sub>n</sub>D; R<sub>1</sub> = alkyl, Ph, phenylalkyl; n = 2-3; m, p = 0-3; D = OH, (substituted) alkoxy, 5-6 member (aromatic) heterocyclyl containing S, O, or N], were prepared Thus, title compound (II; W = S) (multistep preparation from 3-chlorothiophenol and 4-chloronicotinic acid given) inhibited HeLa cells with GI<sub>50</sub> = 0.4  $\mu$ M.

L56 ANSWER 10 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:753467 HCAPLUS

DOCUMENT NUMBER: 139:250903

TITLE: Investigation of Oxygen Interaction with a Pt-Rh/Al<sub>2</sub>O<sub>3</sub> Catalyst by a Differential Temperature-Programmed Desorption Method

AUTHOR(S): Lecomte, J. J.; Haydar, S.; Granger, P.; Leclercq, L.; Leclercq, G.; Joly, J. P.

CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environnement, Universite Claude Bernard Lyon 1, Villeurbanne, 69622, Fr.

SOURCE: Langmuir (2003), 19(22), 9266-9270  
 CODEN: LANGD5; ISSN: 0743-7463

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interaction between gaseous oxygen and a catalyst Pt-Rh supported on  $\gamma$ -Al<sub>2</sub>O<sub>3</sub> (sp. surface area: 100 m<sup>2</sup> g<sup>-1</sup>) was investigated by means of a differential desorption technique called intermittent temperature-programmed desorption (ITPD). Expts. were carried out under conventional secondary vacuum ( $P \approx 10^{-4}$  Pa). Essentially, three desorption steps  $\alpha$ ,  $\beta_1$ , and  $\beta_2$  were observed, occurring around 350, 650, and 750 K, resp. Steps  $\beta_1$  and  $\beta_2$  stem from the desorption of oxygen strongly and dissociatively adsorbed on the metallic particles. Desorption step  $\alpha$  is better observed after oxygen adsorption at ambient temperature; it corresponds to weakly bonded oxygen. The high values of the frequency factors strongly suggest that no readsorption occurred when oxygen desorbed through steps  $\beta_1$  and  $\beta_2$ . Desorption activation

energies for steps  $\beta_1$  and  $\beta_2$  were estimated at 219 and 305 kJ/mol, resp.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 11 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:630052 HCAPLUS

TITLE: Chemo-enzymatic modification of immunosuppressant **cyclosporin A**

AUTHOR(S): Hemenway, Michael H.; Zhang, Qibo; Michels, Peter C.; Rich, Joseph O.; Khmel'nitsky, Yuri L.; Haydar, Simon N.; Molino, Bruce F.

CORPORATE SOURCE: Albany Molecular Research, Inc, Mount Prospect, IL, 60056, USA

SOURCE: Abstracts of Papers, 226th ACS National Meeting, New York, NY, United States, September 7-11, 2003 (2003), BIOL-185. American Chemical Society: Washington, D. C.  
CODEN: 69EKY9

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB **Cyclosporin A** is the most widely prescribed drug for rejection suppression after organ transplantation. However, chronic use of this agent can lead to loss of the transplanted organ due to its nephrotoxicity and neurotoxicity. Decades of investigation have led to the syntheses of more than 3000 **cyclosporin** analogs, but thus far no improved **cyclosporin** analogs has made it to the market. Here we report a chemo-enzymic approach for efficient generation of novel **cyclosporin A** derivs.

L56 ANSWER 12 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:432173 HCAPLUS

TITLE: Biaryl purine derivatives as potent inhibitors of cyclin-E/CDK2, cell growth, and cell cycle progression

AUTHOR(S): Trova, Michael P.; Friedrich, Thomas D.; Alicea, L. R.; Barford, C. A.; Barnes, K. D.; Benanti, T.; Bergeron, M. E.; Bielaska, M.; Bilotta, J. A.; Burry, L. C.; Davidson, M. R.; Duong, T. N.; Haydar, S. N.; Hui, Y.; Johnson, M. R.; Johnson, R. E.; Lu, J.; Murphy, C. M.; O'Grady, H. R.; Peace, D.; Rainka, M. P.; Russell, M.; Salamone, S.; Smith, J. L.; Snider, P. A.; Toporowski, J. W.; Tregay, S. W.; Wilson, A. C.; Wyle, M. J.; Yao, X.; Zheng, X.

CORPORATE SOURCE: Albany Molecular Research, Inc., Albany, NY, USA

SOURCE: Abstracts, 31st Northeast Regional Meeting of the American Chemical Society, Saratoga Springs, NY, United States, June 15-18 (2003), 58. American Chemical Society: Washington, D. C.  
CODEN: 69EBFV

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB A novel series of purine derivs., containing a 6-[(biarylmethyl)amino] substituent, was prepared. The compds. were evaluated in vitro as cyclin/CDK inhibitors and as cell growth inhibitors. We will present the syntheses and structure activity relationships (SARs) of this novel series of analogs. We will also describe some biochem. studies designed to elucidate the effects of these compds. on cell culture. It is expected that compds. with these in vitro and cellular activities may be useful as antitumor agents.

L56 ANSWER 13 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:103597 HCAPLUS  
DOCUMENT NUMBER: 139:182281  
TITLE: Adsorption of p-nitrophenol on an activated carbon with different oxidations  
AUTHOR(S): Haydar, S.; Ferro-Garcia, M. A.; Rivera-Utrilla, J.; Joly, J. P.  
CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environnement, UMR 5634 CNRS-Universite Claude Bernard Lyon 1, Villeurbanne, 69622, Fr.  
SOURCE: Carbon (2003), 41(3), 387-395  
CODEN: CRBNAH; ISSN: 0008-6223  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB An activated carbon prepared from olive stones has been modified through oxidation by nitric acid or sodium hypochlorite. These treatments introduced large amts. of oxygen groups, which were characterized by mass-spectrometry and temperature-programmed desorption. Both CO<sub>2</sub>- and CO-evolving groups were created by these oxidation treatments. A portion of these oxidized specimens was then outgassed under vacuum at  $\leq 823$  K to remove most of the CO<sub>2</sub>-evolving groups from their surface. Oxidized specimens have a smaller surface area than that of the original specimen. Subsequent partial outgassing increases the surface area which, however, does not reach the value it had before oxidation p-Nitrophenol (PNP) adsorption isotherms from aqueous solns. were determined at 298 K for the original, oxidized, and partly outgassed specimens. The results confirm an intermediate plateau at low equilibrium PNP concentration at .apprx.10 mg/L.

The relative effects of textural vs. surface chemical on PNP uptake are then discussed. CO-evolving groups had no influence on PNP uptake. The models in which carbonylic groups are basic adsorption sites for substituted phenols can be ruled out for the entire isotherm of PNP obtained with the original carbon. These models are also unlikely for PNP adsorption on oxidized and partly outgassed specimens.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 14 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:636233 HCAPLUS  
DOCUMENT NUMBER: 138:66809  
TITLE: Risk-directed immunosuppression in heart transplant recipients: maintenance prednisone can be avoided in selected patients  
AUTHOR(S): Arnold, A. N.; Huffman, M.; Eich, D. M.; Bernstein, R. C.; Old, W. D.; Mooney, M.; Szentpetery, S.; Hagberg, R.; McGrath, M.; Rich, J.; Herre, J. M.; Barnhart, G. R.  
CORPORATE SOURCE: Heart Transplant Program, Sentara Norfolk General Hospital, Norfolk, VA, USA  
SOURCE: Transplantation Proceedings (2002), 34(5), 1830-1833  
CODEN: TRPPA8; ISSN: 0041-1345  
PUBLISHER: Elsevier Science Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Patients who received orthotrophic heart transplantation from 1994 to 1998 were studied retrospectively to determine if risk-directed immunosuppression results in good outcome, as measured by patient survival and time to rejection. The study clearly demonstrated that a risk-directed anal. can

select patients for double-drug immunosuppression without maintenance steroids. These selected patients experience severe rejection less frequently and have a patient survival that is similar to patients given triple-drug immunosuppression. The results are obtained without the need for more calcineurin inhibitor or antimetabolite. The improved freedom from severe rejection validates this prospective approach to the selection of a group of patients at lower risk for severe rejection.

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 15 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:136720 HCAPLUS

DOCUMENT NUMBER: 136:401897

TITLE: Recent syntheses of epibatidine. A review

AUTHOR(S): Olivo, Horacio F.; Hemenway, Michael S.

CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA

SOURCE: Organic Preparations and Procedures International (2002), 34(1), 1-26

CODEN: OPPIAK; ISSN: 0030-4948

PUBLISHER: Organic Preparations and Procedures, Inc.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review. The syntheses of epibatidine via cycloaddn. reactions, intramol. nucleophilic displacement reactions and radical cyclizations are discussed.

REFERENCE COUNT: 52 THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 16 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:779595 HCAPLUS

DOCUMENT NUMBER: 136:183752

TITLE: Synthesis of regioisomeric 2,5-bis-substituted-aza-benzothiopyranoindazoles

AUTHOR(S): Krapcho, A. Paul; Haydar, Simon N.

CORPORATE SOURCE: Department of Chemistry, The University of Vermont, Burlington, VT, 05405, USA

SOURCE: Journal of Heterocyclic Chemistry (2001), 38(5), 1153-1166

CODEN: JHTCAD; ISSN: 0022-152X

PUBLISHER: HeteroCorporation

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 136:183752

AB The synthesis of 6-chloro-9-nitro-benzothiopyranopyridin-5-ones (I) has been accomplished. The [3,2-c] analog could not be prepared since attempts to cyclize 3-(2-nitro-5-chlorophenoxy)pyridine-2-carboxylic acid led to the decarboxylation product 3-(2-nitro-5-chlorothiophenoxy) pyridine (40). Treatment of I with substituted hydrazines led to 2-(substituted)-5-nitropyridothiopyranoindazoles. The reduction of the nitro groups of these substrates was effected by treatment with hydrogen gas (palladium catalyst) or by stannous chloride to yield the 5-amino analogs. The conversion of these derivs. to the 2,5-bis(alkylamino)-7-, 8- and 9-aza benzothiopyranoindazoles was accomplished by direct alkylations, acylations, followed by reduction of the amido group with Red-Al or lithium aluminum hydride, or by reductive alkylations in the presence of sodium cyanoborohydride. The removal of the protective BOC-group was effected by treatment of the appropriate substrates with anhydrous hydrogen chloride.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 17 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:455255 HCAPLUS

DOCUMENT NUMBER: 135:195401

TITLE: A regiospecific synthesis of 3,3,6-trimethylindan-1-one

AUTHOR(S): Vogt, Paul F.; Molino, Bruce F.; Robichaud, Albert J.

CORPORATE SOURCE: Department of Medicinal Chemistry, Albany Molecular Research, Inc., Albany, NY, 12203, USA

SOURCE: Synthetic Communications (2001), 31(5), 679-684  
CODEN: SYNCAV; ISSN: 0039-7911

PUBLISHER: Marcel Dekker, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 135:195401

AB A novel, regiospecific synthesis of 3,3,6-trimethylindan-1-one (I) was achieved. The route to I was 6 steps and proceeded in 27% overall yield.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 18 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:390929 HCAPLUS

DOCUMENT NUMBER: 135:65844

TITLE: Sediment discharges in river beds: a potential contribution to environmental standards

AUTHOR(S): Molino, B.; Masi, G.

CORPORATE SOURCE: Dipartimento di Ingegneria e Fisica dell'Ambiente, Universita degli Studi della Basilicata, Romana, 85100, Italy

SOURCE: Ingegneria Ambientale (2000), 29(3/4), 143-148  
CODEN: IGEABH; ISSN: 0394-5871

PUBLISHER: C.I.P.A. Srl

DOCUMENT TYPE: Journal

LANGUAGE: Italian

AB This paper originates from environmental Italian laws anal. relating to the discharge in stream. The laws concern particularly the suspended solid concentration parameter. This also is compared with the same parameter values in International Laws. The Camastra stream (Southern Italy) is monitored by a series of water sampling in different sections and particularly in the river bed downstream from Ponte Fontanelle reservoir to its confluence with the Basento River. The suspended solid concentration during water discharge is monitored.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 19 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:324974 HCAPLUS

DOCUMENT NUMBER: 135:61467

TITLE: Microbial hydroxylation of nitrogen-substituted azabicycloalkanes and its application to a total synthesis of epibatidine

AUTHOR(S): Hemenway, Michael Scott

CORPORATE SOURCE: Univ. of Iowa, Iowa City, IA, USA

SOURCE: (2000) 224 pp. Avail.: UMI, Order No. DA9975820  
From: Diss. Abstr. Int., B 2000, 61(6), 3019

DOCUMENT TYPE: Dissertation

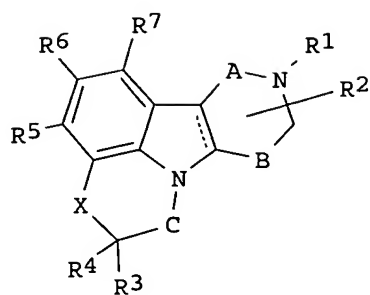
LANGUAGE: English

AB Unavailable

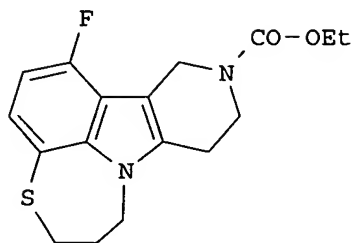


L56 ANSWER 20 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 2000:900647 HCAPLUS  
 DOCUMENT NUMBER: 134:56657  
 TITLE: Preparation of substituted heterocycle fused  
 gamma-carbolines  
 INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei;  
 Mitchell, Ian S.; Haydar, Simon; Chen,  
 Wenting; McClung, Christopher D.; Calvello, Emilie J.  
 B.; Zawrotny, David M.  
 PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA  
 SOURCE: PCT Int. Appl., 764 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077010	A2	20001221	WO 2000-US16373	20000615
WO 2000077010	A3	20010628		
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2373920	AA	20001221	CA 2000-2373920	20000615
EP 1192165	A2	20020403	EP 2000-942807	20000615
EP 1192165	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012411	A	20020416	BR 2000-12411	20000615
TR 200103658	T2	20020621	TR 2001-200103658	20000615
JP 2003502336	T2	20030121	JP 2001-503867	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277055	E	20041015	AT 2000-942807	20000615
ES 2223536	T3	20050301	ES 2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ES 2228549	T3	20050416	ES 2000-941453	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006128	A	20020211	NO 2001-6128	20011214
PRIORITY APPLN. INFO.:			US 1999-139321P	P 19990615
			WO 2000-US16373	W 20000615
OTHER SOURCE(S):		MARPAT 134:56657		
GI				



I



II

AB Novel  $\gamma$ -carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF<sub>3</sub>, alkyl, etc.; R5-R7 = H, halo, CF<sub>3</sub>, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH<sub>2</sub>)<sub>n</sub>, n = 0-3] are prepared. The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions associated with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility. Thus, II is prepared starting from p-fluorophenol,  $\beta$ -propiolactone and 1-carbethoxy-4-piperidone. Pharmaceutical compns. containing I are described.

L56 ANSWER 21 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:900639 HCAPLUS

DOCUMENT NUMBER: 134:56655

TITLE: Preparation of substituted heterocycle fused gamma-carbolines

INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael Guang; Haydar, Simon; Chen, Wenting; McClung, Christopher D.; Calvello, Emilie J. B.; Zawrotny, David M.

PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA

SOURCE: PCT Int. Appl., 308 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

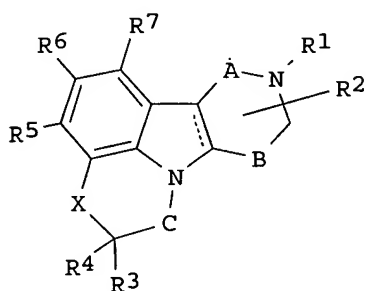
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 5

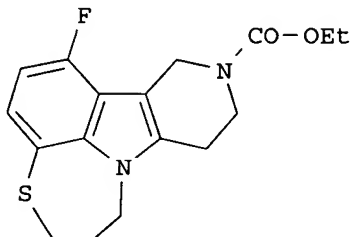
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077002	A1	20001221	WO 2000-US16498	20000615
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2374239	AA	20001221	CA 2000-2374239	20000615
EP 1189904	A1	20020327	EP 2000-941453	20000615
EP 1189904	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

BR 2000012086	A	20020402	BR 2000-12086	20000615
TR 200103658	T2	20020621	TR 2001-200103658	20000615
JP 2003502331	T2	20030121	JP 2001-503860	20000615
NZ 516031	A	20031031	NZ 2000-516031	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277048	E	20041015	AT 2000-941453	20000615
ES 2223536	T3	20050301	ES 2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ES 2228549	T3	20050416	ES 2000-941453	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006116	A	20020211	NO 2001-6116	20011214
PRIORITY APPLN. INFO.:			US 1999-139321P	P 19990615
			WO 2000-US16498	W 20000615
OTHER SOURCE(S):	MARPAT	134:56655		
GI				



I



II

AB Novel  $\gamma$ -carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF3, alkyl, etc.; R5-R7 = H, halo, CF3, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH2) $n$ ,  $n$  = 0-3] are prepared. The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions associated with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility (no data). Thus, II is prepared starting from p-fluorothiophenol,  $\beta$ -propiolactone and 1-carbethoxy-4-piperidone. Pharmaceutical compns. containing I are described.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 22 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:419412 HCAPLUS

DOCUMENT NUMBER: 133:110349

TITLE: Regularities in the temperature-programmed desorption spectra of CO2 and CO from activated carbons

AUTHOR(S): Haydar, S.; Moreno-Castilla, C.; Ferro-Garcia, M. A.; Carrasco-Marin, F.; Rivera-Utrilla, J.; Perrard, A.; Joly, J. P.

CORPORATE SOURCE: Laboratoire d'Application de la Chimie a l'Environnement, UMR 5634 CNRS-Universite Claude Bernard

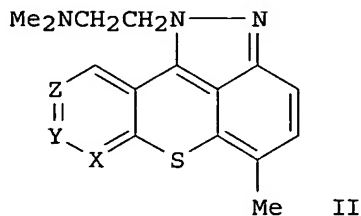
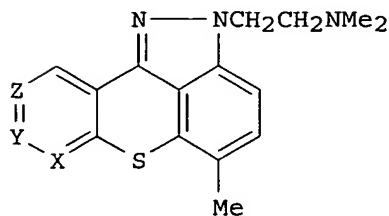
SOURCE: Lyon 1, Villeurbanne, 69622, Fr.  
Carbon (2000), 38(9), 1297-1308  
CODEN: CRBNAH; ISSN: 0008-6223  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Temperature-programmed desorption (TPD) spectra of CO and CO<sub>2</sub> have been obtained

under vacuum or helium flow with activated carbons from different origins and oxidized in various ways. In particular, a special form of TPD, called Intermittent TPD, has been applied to one of the carbon samples (prepared from almond shells and oxidized with nitric acid) in order determine the variation of the apparent activation energy of desorption  $E_d$  as the coverage of the surface decreases. Regularities appeared in the set of results obtained: There are common features in TPD profiles of carbons from different origins and histories. This finding is confirmed by a re-examination of numerous CO and CO<sub>2</sub> spectra found in the literature, including results obtained under ultra-vacuum. These regularities are interpreted by the existence of the same superficial entities (various oxygen groups with different environments).

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 23 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2000:146897 HCAPLUS  
DOCUMENT NUMBER: 132:279149  
TITLE: Synthesis and antitumor activities of 5-methyl-1- and 5-methyl-2-[2-(dimethylamino)ethyl]azabenzothiopyranoidazoles  
AUTHOR(S): Krapcho, A. Paul; Haydar, Simon N.;  
Truong-Chiott, Starlan; Hacker, Miles P.; Menta, E.;  
Beggiolin, G.  
CORPORATE SOURCE: Department of Chemistry, University of Vermont,  
Burlington, VT, 05405, USA  
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000),  
10(3), 305-308  
CODEN: BMCLE8; ISSN: 0960-894X  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB Title compds. I (X = N, Y = Z = CH; Y = N, X = Z = CH; Z = N, X = Y = CH) and II (same X, Y, Z) were prepared. Comparisons of the in vitro antitumor activities of the 2-substituted analogs with the benzothiopyranoidazole chemotypes indicate that positioning the nitrogen atom at C-9 (9-aza analog, Z = N) leads to a substrate with potent antitumor activity. The 1-substituted azabenzothiopyranoidazoles, in comparison with the

corresponding 2-substituted analogs, exhibit a much lower potency.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 24 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:712672 HCAPLUS

DOCUMENT NUMBER: 132:64437

TITLE: Total Synthesis of (+)-Epibatidine Using a Biocatalytic Approach

AUTHOR(S): Olivo, Horacio F.; Hemenway, Michael S.

CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry  
College of Pharmacy and The Center for Biocatalysis  
and Bioprocessing, The University of Iowa, Iowa City,  
IA, 52242, USA

SOURCE: Journal of Organic Chemistry (1999), 64(24), 8968-8969  
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 132:64437

AB (+)-Epibatidine was prepared in 9 steps from trans-4-aminocyclohexanol, via intramol. nucleophilic displacement of a trans-4-aminocyclohexanol derivative, microbial oxidation of an unfunctionalized carbon, and coupling of the chloropyridyl ring to a 7-azanorbornanone.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 25 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:542961 HCAPLUS

TITLE: Microbial hydroxylation of -substituted 7-azabicyclo[2.2.1]heptanes and its application to a total synthesis of epibatidine.

AUTHOR(S): Hemenway, Michael S.; Olivo, Horacio F.

CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry,  
University of Iowa, Iowa City, IA, 52242, USA

SOURCE: Book of Abstracts, 218th ACS National Meeting, New Orleans, Aug. 22-26 (1999), ORGN-575. American Chemical Society: Washington, D. C.  
CODEN: 67ZJA5

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB A total synthesis of the natural product and potent non-opioid analgesic epibatidine has been pursued, starting from com. available trans-1,4-aminocyclohexanol hydrochloride, and utilizing microbial hydroxylation via Beauveria bassiana as the key step. A variety of N-substituents have been explored in the hydroxylation step. The hydroxylated metabolite(s) has proved to be a valuable intermediate in this biocatalytic approach to epibatidine. Details concerning the progress toward obtaining epibatidine will be discussed.

L56 ANSWER 26 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:469257 HCAPLUS

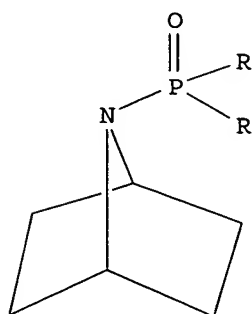
DOCUMENT NUMBER: 131:228758

TITLE: Syntheses of New Phosphorus-Containing Azabicycloalkanes and Their Microbial Hydroxylation Using Beauveria bassiana

AUTHOR(S): Hemenway, Michael S.; Olivo, Horacio F.

CORPORATE SOURCE: Division of Medicinal Natural Products Chemistry  
College of Pharmacy and The Center for Biocatalysis  
and Bioprocessing, The University of Iowa, Iowa City,

SOURCE: IA, 52242, USA  
 Journal of Organic Chemistry (1999), 64(17), 6312-6318  
 CODEN: JOCEAH; ISSN: 0022-3263  
 PUBLISHER: American Chemical Society  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 131:228758  
 GI



I

AB Representative novel phosphorus-containing azabicyclic substrates I (R = OEt, OPh, Ph) have been synthesized and subsequently microbially hydroxylated in fair to good yields using the microorganism *Beauveria bassiana*. (7-Azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Et ester was hydroxylated at the unactivated methylene carbon to give (2-endo-hydroxy-7-azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Et ester in 43% yield and 64% ee, while N-(diphenylphosphinoyl)-7-azabicyclo[2.2.1]heptane was similarly hydroxylated to give 2-endo-hydroxy-7-(diphenylphosphinoyl)-7-azabicyclo[2.2.1]heptane in 35% yield and 20% ee. (7-Azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Ph ester yielded two distinct hydroxylated products: monohydroxylated (2-endo-hydroxy-7-azabicyclo[2.2.1]hept-7-yl)phosphonic acid di-Ph ester in 7% yield and 7% ee and dihydroxylated (2-endo-hydroxy-7-azabicyclo[2.2.1]hept-7-yl)phosphonic acid Ph, p-hydroxyphenyl ester in 37% yield and 77% ee. HPLC studies indicated that the monohydroxylated metabolite is formed first during fermentation, and becomes a substrate for a second enzymic hydroxylation at one of the aromatic rings with induced enantioselection, to give the dihydroxylated metabolite. All microbially hydroxylated metabolites were easily N-deprotected using TFA-CH<sub>2</sub>Cl<sub>2</sub> (1:1). Thus, N-phosphinyl groups are good facilitators of hydroxylation reactions with *B. bassiana* and offer a new choice for an N-substituent when substrates are hydroxylated with this microorganism. By offering a new N-substituent, this work extends the general utility of *B. bassiana* as a preparatively useful unactivated methylene hydroxylator.

REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L56 ANSWER 27 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1999:298770 HCAPLUS

DOCUMENT NUMBER: 131:130150

TITLE: Syntheses of New Open-Ring and homo-Epibatidine  
 Analogs from Tropinone



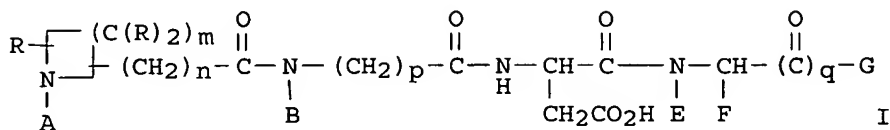
MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,  
TD, TG

US 5780590	A	19980714	US 1996-700950	19960821
US 6274705	B1	20010814	US 1998-137998	19980821
US 2002002268	A1	20020103	US 2001-903813	20010712
US 6797700	B2	20040928		

PRIORITY APPLN. INFO.:

US 1993-138820	B2 19931015
WO 1994-US12135	W 19941017
US 1993-13820	B2 19931015
US 1995-476750	A2 19950607
US 1996-628648	A1 19960502
US 1998-137998	A3 19980821

OTHER SOURCE(S) : MARPAT 130:153977  
GI



AB Title compds. [I; R = H, alkyl, aryl, aralkyl; A = H, (substituted) amidino; B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; E = H; EF = atoms to form 4-7 membered azacycloalkane ring; F = H, side chain of a naturally occurring  $\alpha$ -amino acid, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, (substituted) aryl, (substituted) aralkyl, (substituted) heterocyclyl, (substituted) heterocyclylalkyl; G = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, (substituted) aryl, (substituted) aralkyl, (substituted) heterocyclyl, (substituted) heterocyclylalkyl, OR1, NR1R2; R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; q = 0, 1; m = 1-5; n = 0-6; p = 1-4] were prepared For example, N-[N-[N-(4-(piperidin-4-yl)butanoyl)-N-ethylglycyl]aspartyl]- $\beta$ -cyclohexylalanine was prepared from BocN(Et)CH<sub>2</sub>CO<sub>2</sub>H, Boc-Asp(OCH<sub>2</sub>Ph)-OH,  $\beta$ -cyclohexylalanine and Me 4-(N-Boc-piperidine-4-yl)crotonate using solution phase procedures. Platelet aggregation and fibrinogen-binding assays were performed on I (incomplete data).

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 29 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:762441 HCAPLUS

DOCUMENT NUMBER: 130:57581

TITLE: Study of the evolution of carbon dioxide from active carbon by a threshold temperature-programmed desorption method

AUTHOR(S) : Haydar, S.; Joly, J. P.

CORPORATE SOURCE: Laboratoire d'Application de la Chimie a  
l'Environnement (UMR 5634), CNRS-Universite Claude  
Bernard Lyon 1, Villeurbanne, 69622, Fr.

SOURCE: Journal of Thermal Analysis and Calorimetry (1998),  
52(2), 345-353

CODEN: JTACF7; ISSN: 1418-2874

PUBLISHER: Kluwer Academic Publishers



DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A particular Temperature-Programmed Desorption (TPD) method, called 'Intermittent TPD', has been applied to the decomposition of oxygen groups naturally present at the surface of a microporous active carbon. It is shown that this method provides more information on the kinetics of the thermal decomposition of these species than the classical TPD technique. The main result is that the decomposition of these oxygen groups occurs in at least 7 distinct stages which have been characterized by their apparent activation energy and the corresponding frequency factor. The present study underlines the usefulness of ITPD for studying the rate of desorption of gases from powdered samples with a strongly heterogeneous surface.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 30 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:699917 HCAPLUS

DOCUMENT NUMBER: 130:24947

TITLE: Unexpected displacements of chloride by bromide found during Sandmeyer reactions of 3- or 5-amino-2-chloropyridines

AUTHOR(S): Krapcho, A. Paul; Haydar, Simon N.

CORPORATE SOURCE: Department of Chemistry, The University of Vermont, Burlington, VT, 05405, USA

SOURCE: Heterocyclic Communications (1998), 4(4), 291-292  
CODEN: HCOMEX; ISSN: 0793-0283

PUBLISHER: Freund Publishing House Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Facile, temperature dependent displacements of chloride by bromide have been found in the diazotizations of 3-amino-2-chloropyridine or 5-amino-2-chloropyridine, followed by addition of CuBr in 48% HBr, which lead to good yields of the unexpected 2,3-dibromopyridine or 2,5-dibromopyridine, resp.

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 31 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:479050 HCAPLUS

DOCUMENT NUMBER: 129:122869

TITLE: Antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides

INVENTOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SOURCE: U.S., 29 pp., Cont.-in-part of U.S. Ser. No. 476,750.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5780590	A	19980714	US 1996-700950	19960821
US 5866685	A	19990202	US 1996-628648	19960502
CA 2263732	AA	19980430	CA 1997-2263732	19970815
WO 9817678	A1	19980430	WO 1997-US14578	19970815

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,  
 LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,  
 PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,  
 UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
 RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
 GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
 GN, ML, MR, NE, SN, TD, TG

AU 9740749	A1	19980515	AU 1997-40749	19970815
AU 722112	B2	20000720		
EP 929572	A1	19990721	EP 1997-938424	19970815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9711205	A	19990817	BR 1997-11205	19970815
CN 1231671	A	19991013	CN 1997-198164	19970815
NZ 334059	A	20000128	NZ 1997-334059	19970815
AP 904	A	20001124	AP 1999-1452	19970815
W: GH, KE, LS, MW, SD, SZ, UG, ZW				
JP 2001501965	T2	20010213	JP 1998-519340	19970815
ZA 9707511	A	19980303	ZA 1997-7511	19970821
KR 2000035797	A	20000626	KR 1999-701363	19990219
NO 9900836	A	19990420	NO 1999-836	19990222

PRIORITY APPLN. INFO.:

US 1993-138820	B2	19931015
US 1995-476750	A2	19950607
US 1996-628648	A1	19960502
WO 1994-US12135	W	19941017
US 1996-700950	A	19960821
WO 1997-US14578	W	19970815

OTHER SOURCE(S): MARPAT 129:122869

AB Peptides P2NB(CH<sub>2</sub>)pCONHCH(CH<sub>2</sub>CO<sub>2</sub>P<sub>1</sub>)CONE1CHE2COG [B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylalkyl; E<sub>1</sub> = H or E<sub>1</sub>NCH<sub>2</sub> is azacycloalkyl; E<sub>2</sub> = α-carbon side chain of a naturally occurring α-amino acid, H, alkyl, cycloalkyl, aryl, etc.; G = OR<sub>1</sub> or NR<sub>1</sub>R<sub>2</sub> (R<sub>1</sub>, R<sub>2</sub> = H, alkyl, cycloalkyl, aryl, etc.); p = 1-4; P<sub>1</sub> is a hydrogenation labile acid protecting group; P<sub>2</sub> is an acid labile amine protecting group or TFA, H] were prepared as antithrombotics. N-[N-[N-(4-piperidin-4-yl)butanoyl]-N-ethylglycyl]-L-aspartyl]-L-β-cyclohexylalaninamide was prepared and had IC<sub>50</sub> = 0.097 μM for inhibition of platelet aggregation.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 32 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:429224 HCAPLUS

DOCUMENT NUMBER: 129:49374

TITLE: Design of a New Class of Orally Active Fibrinogen Receptor Antagonists

AUTHOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.; Chu, Valeria; Brown, Karen; Sabatino, Ralph D.; Bostwick, Jeffrey S.; Kasiewski, Charles; Bentley, Ross; Windisch, Vincent; Perrone, Mark; Dunwiddie, Christopher T.; Leadley, Robert J.

CORPORATE SOURCE: Department of Cardiovascular Research, Rhone-Poulenc Rorer Central Research, Collegeville, PA, 19426, USA

SOURCE: Journal of Medicinal Chemistry (1998), 41(14), 2492-2502

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The integrin receptor recognition sequence Arg-Gly-Asp was successfully

used as a template from which to develop a series of potent, selective, orally active, peptide-based fibrinogen receptor antagonists with a long duration of action. Simple modifications centered on the Arg and Gly residues quickly led to a modified peptide, R(CH<sub>2</sub>)<sub>n</sub>CONEtCH<sub>2</sub>CO-L-Asp-L-Val-OH [I, R = NHC(:NH)NH<sub>2</sub>, n = 5, II] with significantly enhanced ability to inhibit in vitro platelet aggregation. Substitution of the guanidino group in II provided I [R = 4-piperidinyl, n = 3] which showed not only further increase in potency but also a modest degree of oral efficacy. Finally, exploration of the nature of the C-terminal amino acid, with respect to its side-chain functionality and the carboxy terminus, yielded a group of mols. that showed excellent in vitro potency for inhibiting platelet aggregation, excellent integrin selectivity, a high level of oral efficacy, and an extended duration of action.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 33 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:268512 HCAPLUS

DOCUMENT NUMBER: 129:4865

TITLE: Preparation of antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides

INVENTOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA; Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.

SOURCE: PCT Int. Appl., 63 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9817678	A1	19980430	WO 1997-US14578	19970815
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5780590	A	19980714	US 1996-700950	19960821
CA 2263732	AA	19980430	CA 1997-2263732	19970815
AU 9740749	A1	19980515	AU 1997-40749	19970815
AU 722112	B2	20000720		
EP 929572	A1	19990721	EP 1997-938424	19970815
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
BR 9711205	A	19990817	BR 1997-11205	19970815
NZ 334059	A	20000128	NZ 1997-334059	19970815
AP 904	A	20001124	AP 1999-1452	19970815
W: GH, KE, LS, MW, SD, SZ, UG, ZW				
JP 2001501965	T2	20010213	JP 1998-519340	19970815
NO 9900836	A	19990420	NO 1999-836	19990222
PRIORITY APPLN. INFO.:			US 1996-700950	A 19960821
			US 1993-138820	B2 19931015
			US 1995-476750	A2 19950607

US 1996-628648 A1 19960502  
WO 1997-US14578 W 19970815

OTHER SOURCE(S): MARPAT 129:4865

AB The invention is directed to a non-hygroscopic stable crystalline form of the antithrombotic compound N-[N-[N-[4-(piperidin-4-yl)butanoyl]-N-ethylglycyl]-L-aspartyl]-L-β-cyclohexyl-alanine amide (I), to processes for preparing said stable crystalline form, to a pharmaceutical composition thereof, and intermediates thereof. The invention is directed also to processes and intermediates for preparing a compound of formula P2'N(B)(CH2)pCONHCH(CH2CO2P1)CON(E1)CH(E2)COG [B = alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkylalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; E1 = H; E2 = the α-carbon side chain of a naturally occurring α-amino acid, H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, (un)substituted aryl, (un)substituted aralkyl, (un)substituted heterocyclyl, (un)substituted heterocyclylalkyl; or E1 and E2 taken together with the nitrogen and carbon atoms through which E1 and E2 are linked form a 4-, 5-, 6-, or 7-membered ring; G = OR1, NR1R2; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, alkylcycloalkyl, alkylcycloalkyl, aryl, aralkyl, alkylaryl, alkylaralkyl; p = 1-4; P1 = a hydrogenation-labile acid protecting group; P2' = P2, CF3CO2H.H; P2 = an acid-labile amine protecting group]. Thus, 4-(1-benzyloxycarbonyl-4-piperidinylene)butyric acid (preparation given) was condensed with Et-Gly-Asp(OBzl)-Cha-NH2.CF3CO2H (Cha = β-cyclohexyl-L-alanine) using (2-1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate and (Me2CH)2NEt in DMF to give RNEtCH2CO-Asp(OBzl)-Cha-NH2 [R = 4-(1-benzyloxycarbonyl-4-piperidinylene)butyryl] in 83% yield, which was hydrogenated by ammonium formate in the presence of 10% Pd-C in a mixture of EtOH, iPrOH, and H2O at 40-50° for 5 h to give hygroscopic crystalline form of I in 84.8% yield. Hygroscopic crystalline form of I (7.45 kg) was milled in a hammer mill. The resulting solid (7.35 kg) was placed in a stainless steel drier tray and the tray was covered with perforated aluminum foil, then sealed into a humidity oven, kept sealed throughout the form conversion at 40%RH and 60° for 1 h, 80% RH and 60° for 12 h, and then at 40% RH and 60° for 2 h to give non-hygroscopic crystalline form of I in 96.6% yield. I showed IC50 of 0.097 μM for inhibiting human fibrinogen-induced aggregation of human platelet vs. 0.047 μM for N-[4-(4-piperidyl)butanoyl]-glycyl-L-aspartyl-L-tryptophan.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 34 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:178676 HCAPLUS

DOCUMENT NUMBER: 128:282744

TITLE: New preparation of activated 2-vinylaziridines from δ-amino alcohols

AUTHOR(S): Olivo, Horacio F.; Hemenway, Michael S.; Hartwig, Amy C.; Chan, Raymond

CORPORATE SOURCE: Division Medicinal Natural Products Chemistry, College Pharmacy, University Iowa, Iowa City, IA, 52242, USA

SOURCE: Synlett (1998), (3), 247-248  
CODEN: SYNLES; ISSN: 0936-5214

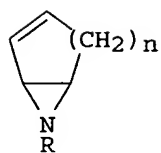
PUBLISHER: Georg Thieme Verlag

DOCUMENT TYPE: Journal

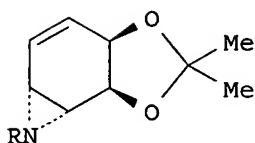
LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:282744

GI



I



II

AB Activated vinylaziridines I (R = PhCO, n = 1-3; R = PhCH<sub>2</sub>O<sub>2</sub>C, n = 2; R = 4-tosyl, n = 2) and II (R = PhCO, PhCH<sub>2</sub>O<sub>2</sub>C, Me<sub>3</sub>CO<sub>2</sub>C) were prepared from appropriate cis-1-aminocycloalk-2-en-4-ols by using Mitsunobu conditions.

L56 ANSWER 35 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1998:160361 HCAPLUS

DOCUMENT NUMBER: 128:230549

TITLE: Synthesis and microbial hydroxylation of some azabicycloalkanes

AUTHOR(S): Olivo, Horacio F.; Hemenway, Michael S.; Gezginci, Mikail H.

CORPORATE SOURCE: Division of Medicinal and Natural Products Chemistry, College of Pharmacy, The University of Iowa, Iowa City, IA, 52242, USA

SOURCE: Tetrahedron Letters (1998), 39(11), 1309-1312

CODEN: TELEAY; ISSN: 0040-4039

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 128:230549

GI



I

AB N-Substituted 7-azabicyclo[2.2.1]heptanes, e.g. I, were synthesized in a short route. These compds. containing benzamide or benzenesulfonamide groups are good substrates for microbial oxidation of unactivated carbons by B. bassiana.

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 36 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:752575 HCAPLUS

DOCUMENT NUMBER: 128:84036

TITLE: Conformationally flexible platelet aggregation inhibitors based on the tetrapeptide Arg-Gly-Asp-Arg

AUTHOR(S): Klein, S. I.; Czekaj, M.; Molino, B. F.; Chu, V.

CORPORATE SOURCE: Department of Cardiovascular Research, Rhone-Poulenc Rorer, Collegeville, PA, 19426, USA

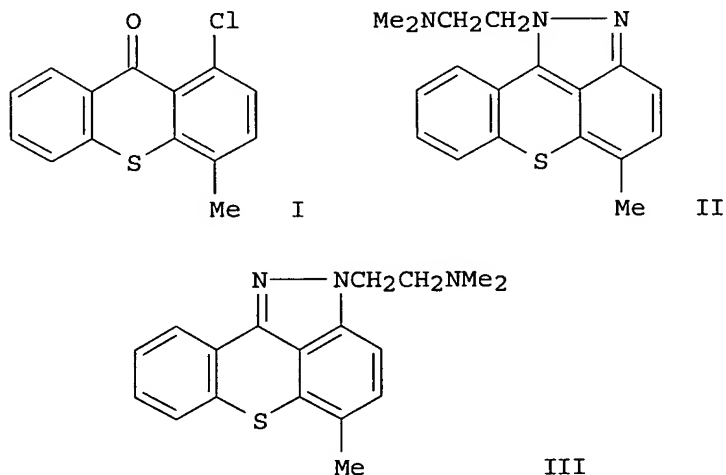
SOURCE: European Journal of Medicinal Chemistry (1997),

32(10), 833-839

CODEN: EJMCA5; ISSN: 0223-5234

PUBLISHER: Editions Scientifiques et Medicales Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A series of nonpeptide fibrinogen receptor antagonists based upon the tetrapeptide Arg-Gly-Asp-Arg were prepared. These relatively simple derivs. incorporate a high degree of conformational flexibility that was anticipated to allow them to attain the requisite conformation for binding to the platelet fibrinogen receptor. Optimization of the distances between the required acidic and basic functional groups led eventually to compound which is a 100-fold more potent inhibitor of platelet aggregation than the peptide it is based upon.  
 REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

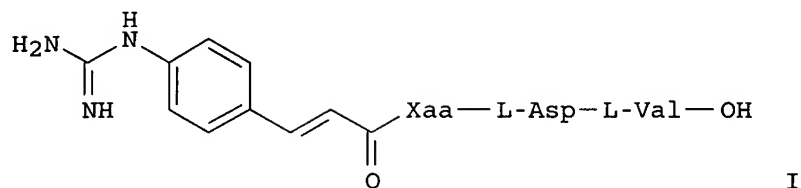
L56 ANSWER 37 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1997:751985 HCAPLUS  
 DOCUMENT NUMBER: 128:48170  
 TITLE: N,N,5-Trimethyl-1H-[1]benzothiopyrano[4,3,2-cd]indazole-1-ethanamine - a novel heterocycle  
 AUTHOR(S): Krapcho, A. Paul; Haydar, Simon N.  
 CORPORATE SOURCE: Department of Chemistry, University of Vermont, Burlington, VT, 05405, USA  
 SOURCE: Journal of Heterocyclic Chemistry (1997), 34(5), 1637-1638  
 CODEN: JHTCAD; ISSN: 0022-152X  
 PUBLISHER: HeteroCorporation  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB Treatment of thioxanthenone I with [2-(dimethylamino)ethyl]hydrazine led to benzothiopyranoindazole II, a novel heterocycle, along with its expected isomer (III).  
 REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 38 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1997:469001 HCAPLUS  
 DOCUMENT NUMBER: 127:162104

TITLE: Constrained  $\beta$ -alanine based GpIIb/IIIa antagonists  
 AUTHOR(S): Klein, Scott I.; Czekaj, Mark; Molino, Bruce F.; Chu, Valeria  
 CORPORATE SOURCE: Rhone-Poulenc Rorer, Departments of Cardiovascular Chemistry and Biology, Collegeville, PA, 19426, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(13), 1773-1778  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB A series of novel fibrinogen receptor antagonists, e.g. I (Xaa = N-Et  $\beta$ -alanine, (R)-2-pyrrolidineacetic acid, (R)-2-piperidineacetic acid, (S)-3-pyrrolidinecarboxylic acid, (S)-2-azetidineacetic acid) has been synthesized following the design principles of centrally constrained and peptide based fibrinogen receptor antagonists. The centrally constrained  $\beta$ -alanine based RGD mimics I have been demonstrated to be potent inhibitors of platelet aggregation.

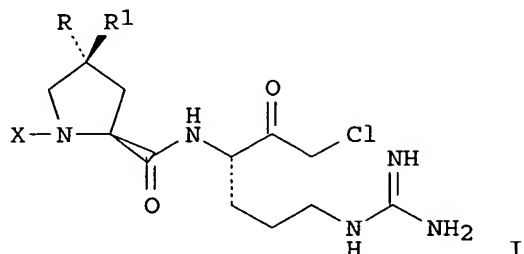
REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 39 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1997:162128 HCAPLUS  
 TITLE: Regioisomeric azabenzothiopyranoindazoles. Synthesis and antitumor evaluations.  
 AUTHOR(S): Krapcho, A. Paul; Haydar, Simon N.; Hacker, Miles P.; Truong-Chiott, Starlan; Menta, Ernesto  
 CORPORATE SOURCE: Department Chemistry, University Vermont, Burlington, VT, 05405, USA  
 SOURCE: Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17 (1997), MEDI-296. American Chemical Society: Washington, D. C.  
 CODEN: 64AOAA  
 DOCUMENT TYPE: Conference; Meeting Abstract  
 LANGUAGE: English

AB A number of benzothiopyranoindazoles have been synthesized in order to avoid enzymically mediated radical cycling and specific chemotypes exhibited broad-spectrum antitumor activities. As part of a program to develop new chemotypes, we have replaced the carbon atom of the benzothiopyranoindazole skeleton at positions 7, 8 and 9 with a nitrogen atom leading to the 7-aza-, 8-aza- and 9-azabenzothiopyranoindazoles. The synthesis of the 10-aza regioisomer is currently under investigation. The antitumor activities, which are highly dependent on the position of the nitrogen atom and the side arm structure (R and R1), will be discussed. Several promising candidates for preclin. trials have been identified.

L56 ANSWER 40 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:604560 HCAPLUS  
 DOCUMENT NUMBER: 125:301564  
 TITLE: O-benzyl hydroxyproline as a bioisostere for Phe-Pro:  
 Novel dipeptide thrombin inhibitors  
 AUTHOR(S): Klein, Scott I.; Dener, Jeffrey M.; **Molino, Bruce F.**; Gardner, Charles J.; D'Alisa, Rose;  
 Dunwiddie, Christopher T.; Kasiewski, Charles;  
 Leadley, Robert J.  
 CORPORATE SOURCE: Department Medicinal Chemistry, Rhone-Poulenc Rorer,  
 Collegeville, PA, 19426, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1996),  
 6(18), 2225-2230  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB A series of thrombin inhibitors I [X = H-D-Phe, Ph(CH<sub>2</sub>)<sub>2</sub>CO, Ac, Et, MeSO<sub>2</sub>; R = H, PhCH<sub>2</sub>O, cyclohexylmethoxy, BuO, Ph(CH<sub>2</sub>)<sub>3</sub>O, Ph<sub>2</sub>CH(CH<sub>2</sub>)<sub>2</sub>O; R<sub>1</sub> = H, OCH<sub>2</sub>Ph], based on the known inhibitor PPACK (I; X = H-D-Phe, R = R<sub>1</sub> = H) in which the D-Phe-Pro dipeptide has been replaced, were prepared and tested. I (X = Ac, R = PhCH<sub>2</sub>O, R<sub>1</sub> = H) is a more potent inhibitor of thrombin, and is more selective, than PPACK itself.

L56 ANSWER 41 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1996:398914 HCAPLUS  
 DOCUMENT NUMBER: 125:131632  
 TITLE: Non-peptide fibrinogen receptor antagonists based upon  
 a 4-substituted piperidine scaffold  
 AUTHOR(S): Klein, Scott; **Molino, Bruce F.**; Czekaj,  
 Mark; Dener, Jeffrey S.; Leadley, Robert J.; Sabatino,  
 Ralph; Dunwiddie, Christopher T.; Chu, Valeria  
 CORPORATE SOURCE: Rhone-Poulenc Rorer, Dep. Medicinal Chem.,  
 Collegeville, PA, 19426, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1996),  
 6(12), 1403-1408  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 125:131632

AB Structure-activity relationships developed from work with peptide based fibrinogen receptor antagonists have been successfully applied to the development of simple and highly potent nonpeptide agents of the same class.



L56 ANSWER 42 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:389613 HCAPLUS

DOCUMENT NUMBER: 125:66726

TITLE: An integrated approach to observe the evolution of pollutants in reservoirs

AUTHOR(S): Copertino, V.A.; de Bernardinis, B.; Molino, B.; Telesca, V.; Singh, V.P.

CORPORATE SOURCE: Department of Engineering and Environmental Physics, University of Basilicata, Potenza, 85100, Italy

SOURCE: Water Science and Technology Library (1996), 16(Vol. 3, Water-Quality Hydrology), 43-55

CODEN: WSTLEQ; ISSN: 0921-092X

PUBLISHER: Kluwer

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A method for combining monitoring, math. modeling, and the use of a geog. information system (GIS) is proposed to investigate the transport, dispersion and diffusion of pollutants in reservoirs. Preliminary and partial results obtained from an extensive and continuous observation and measurement activity on the Camastra reservoir have confirmed the validity of the proposed approach.

L56 ANSWER 43 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:968156 HCAPLUS

DOCUMENT NUMBER: 124:41821

TITLE: Bis(5-chloro-2-nitrophenyl) disulfide

AUTHOR(S): Garcia, J. Gabriel; Haydar, Simon N.; Krapcho, A. Paul; Fronczek, Frank R.

CORPORATE SOURCE: Dep. Chem., Univ. Vermont, Burlington, VT, 05405-0125, USA

SOURCE: Acta Crystallographica, Section C: Crystal Structure Communications (1995), C51(11), 2333-5

CODEN: ACSCEE; ISSN: 0108-2701

PUBLISHER: Munksgaard

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The title mol.,  $C_{12}H_6Cl_2N_2O_4S_2$ , lies on a 2-fold axis in the crystal. The C-S-S-C group has a skewed nonplanar conformation with a torsion-angle magnitude of  $86.7(1)^\circ$ . The S-S-C bond angle is  $104.11(5)^\circ$ , and the S-S, S-C, C-N, and C-Cl bond lengths are  $2.0432(5)$ ,  $1.789(1)$ ,  $1.462(2)$  and  $1.726(1)$  Å, resp. The nitro group is rotated  $15.2(2)^\circ$  out of the plane of the Ph ring. Crystallog. data and atomic coordinates are given.

L56 ANSWER 44 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:886373 HCAPLUS

DOCUMENT NUMBER: 123:306599

TITLE: Antithrombotic azacycloalkylalkanoyl peptides and pseudopeptides

INVENTOR(S): Klein, Scott I.; Molino, Bruce F.

PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA

SOURCE: PCT Int. Appl., 58 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.

KIND

DATE

APPLICATION NO.

DATE

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WO 9510295          A1      19950420      WO 1994-US12135      19941017
W:  AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB,
    GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW,
    NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU,
    MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN,
    TD, TG
CA 2174097          AA      19950420      CA 1994-2174097      19941017
CA 2174097          C       20020604
HU 73856            A2      19960930      HU 1996-983          19941017
CN 1135717          A       19961113      CN 1994-194242       19941017
BR 9407839          A       19970513      BR 1994-7839         19941017
EP 812205           A1      19971217      EP 1995-900403       19941017
EP 812205           B1      20010314
R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE
AU 703854           B2      19990401      AU 1994-81237        19941017
AU 9481237          A1      19950504
RU 2134695          C1      19990820      RU 1996-109375       19941017
RO 115520           B1      20000330      RO 1996-812          19941017
JP 3032297          B2      20000410      JP 1995-512250       19941017
JP 09507213         T2      19970722
AT 199727           E       20010315      AT 1995-900403       19941017
ES 2155122          T3      20010501      ES 1995-900403       19941017
PT 812205           T       20010830      PT 1995-900403       19941017
PL 181749           B1      20010928      PL 1994-313975       19941017
CZ 291378           B6      20030212      CZ 1996-1084         19941017
FI 9601634          A       19960523      FI 1996-1634         19960412
NO 9601460          A       19960617      NO 1996-1460         19960412
BG 63166            B1      20010531      BG 1996-100544       19960426
US 5866685          A       19990202      US 1996-628648       19960502
HK 1006225          A1      20011207      HK 1998-105458       19980616
US 6274705          B1      20010814      US 1998-137998       19980821
GR 3035581          T3      20010629      GR 2001-400194       20010315
US 2002002268       A1      20020103      US 2001-903813       20010712
US 6797700          B2      20040928
PRIORITY APPLN. INFO.:
US 1993-138820      A       19931015
US 1993-13820       B2      19931015
WO 1994-US12135     W       19941017
US 1996-628648      A1      19960502
US 1998-137998      A3      19980821

OTHER SOURCE(S):      MARPAT 123:306599
AB  The present invention relates to azacycloalkylalkanoyl peptides and
pseudopeptides which inhibit platelet aggregation and thrombus formation
thereby being useful in the prevention and treatment of thrombosis associated
with disease states such as myocardial infarction, stroke, peripheral
arterial disease, and disseminated intravascular coagulation, to methods
for the prevention or treatment of thrombosis in a mammal in need of such
therapy comprising the administration of a therapeutically effective amount
of such compds., and to pharmaceutical compns. comprising such compds.

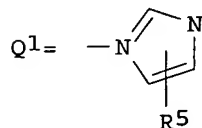
L56  ANSWER 45 OF 77  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:    1995:511411  HCAPLUS
DOCUMENT NUMBER:     122:291536
TITLE:               Preparation of antithrombotic peptides and
pseudopeptides.
INVENTOR(S):         Klein, Scott I.; Molino, Bruce F.; Czekaj,
Mark; Gardner, Charles; Becker, Michael R.; Dener,
Jeffrey M.; Pelletier, Jeffrey C.
PATENT ASSIGNEE(S):  USA

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SOURCE: U.S., 24 pp. Cont.-in-part of U.S. Ser. No. 677,006, abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5332726	A	19940726	US 1992-859779	19920330
US 4952562	A	19900828	US 1989-415006	19890929
PRIORITY APPLN. INFO.:			US 1989-415006	A2 19890929
			US 1990-460777	B2 19900104
			US 1990-534385	B2 19900607
			US 1991-677006	B2 19910328

OTHER SOURCE(S): MARPAT 122:291536  
 GI



AB A(CH<sub>2</sub>)<sub>m1</sub>(CR<sub>1</sub>R<sub>2</sub>)h<sub>1</sub>Bk(CR<sub>3</sub>R<sub>4</sub>)h<sub>2</sub>(CH<sub>2</sub>)<sub>m2</sub>DCH[(CH<sub>2</sub>)<sub>n</sub>CO<sub>2</sub>H]COZ [A = cyano, Q<sup>1</sup>, (NH)x<sub>C</sub>(N:R<sub>5</sub>)(NH)x<sub>1</sub>R<sub>6</sub>, etc.; B, D = CH<sub>2</sub>NH, CH<sub>2</sub>S, CH<sub>2</sub>O, etc.; Z = OR<sub>6</sub>, N-containing heterocyclyl, amino acid or dipeptide residue, etc.; R<sub>1</sub>-R<sub>6</sub> = H, alkyl, cycloalkyl, cycloalkylmethyl, (substituted) aryl, aralkyl; h<sub>1</sub>, h<sub>2</sub>, k = 0,1; m<sub>1</sub>, m<sub>2</sub> = 0-9; n = 1-3; x, x<sub>1</sub> = 0,1], were prepared Thus, arginylglycylaspartylisobutylamide (solution phase preparation given) inhibited fibrinogen-mediated platelet aggregation with IC<sub>50</sub> = 3.6 μM.

L56 ANSWER 46 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:64620 HCAPLUS

DOCUMENT NUMBER: 122:23449

TITLE: Antithrombotic activity of a linear conformationally flexible RGD mimic

AUTHOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Chu, Valeria; Ruggeri, Zaverio; Cook, Jacquelynn J.; Bostwick, Jeffrey S.; Kasiewski, Charles

CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, 19426, USA

SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993), Meeting Date 1992, 635-6. Editor(s): Schneider, Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth. CODEN: 60LUAN

DOCUMENT TYPE: Conference

LANGUAGE: English

AB Elimination of the terminal amino group, lengthening of the arginine side chain by one C atom, and N-alkylation of the Arg-Gly amide bond provided an analog of the parent peptide RGDV, RG 13965. RG 13965 represents a relatively simple and highly effective class of peptide-derived antithrombotic agents which may prove to be clin. useful.

L56 ANSWER 47 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:646328 HCAPLUS  
DOCUMENT NUMBER: 121:246328  
TITLE: Compounds having cholecystokinin and gastrin  
antagonistic properties  
INVENTOR(S): Ewing, William R.; **Molino, Bruce F.**  
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals Inc., USA  
SOURCE: U.S., 16 pp.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5340801	A	19940823	US 1991-697177	19910508
PRIORITY APPLN. INFO.:			US 1991-697177	19910508
OTHER SOURCE(S):	MARPAT 121:246328			

AB This invention relates to preparation of N-arylcarbamoylproline analogs which are useful as cholecystokinin and gastrin antagonists and their use in preventing or treating cholecystokinin- or gastrin-related disorders of the gastrointestinal, central nervous, or appetite regulatory systems. For example, 2-[[N-(3-methyl)phenylcarbamoyl-4R-benzyloxy]-L-prolyl]-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole was prepared by 3 steps from N- $\alpha$ -tert-butoxycarbonyl-O-benzyl-L-4-hydroxyproline and 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole and subjected for in vitro CCK-A receptor and gastrin receptor binding assays.

L56 ANSWER 48 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:622204 HCAPLUS  
DOCUMENT NUMBER: 121:222204  
TITLE: Highly potent and selective gastrin receptor  
antagonists based on CCK-4  
AUTHOR(S): Ewing, W. Richard; **Molino, Bruce F.**; Bolton,  
Scott A.; Manetta, Vincent; Pendley, Charles;  
Capilino, Alison  
CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., Collegeville, PA,  
19426, USA  
SOURCE: Pept. 1992, Proc. Eur. Pept. Symp., 22nd (1993),  
Meeting Date 1992, 619-20. Editor(s): Schneider,  
Conrad H.; Eberle, Alex N. ESCOM: Leiden, Neth.  
CODEN: 60LUAN  
DOCUMENT TYPE: Conference  
LANGUAGE: English

AB Effects were investigated of substituting the C-terminal Asp on a CCK-4-based gastrin receptor antagonist. Cyclic diacids gave more potent antagonists and displayed better selectivity for the gastrin receptor over the CCK-A receptor.

L56 ANSWER 49 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:670633 HCAPLUS  
DOCUMENT NUMBER: 119:270633  
TITLE: Preparation of antithrombotic diaminoalkanoic acid  
derivatives  
INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**  
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer International (Holdings) Inc., USA  
SOURCE: PCT Int. Appl., 30 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent

LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9311759	A1	19930624	WO 1992-US10535	19921207
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 5258398	A	19931102	US 1991-808400	19911216
AU 9332421	A1	19930719	AU 1993-32421	19921207
PRIORITY APPLN. INFO.:			US 1991-808400	A 19911216
			WO 1992-US10535	A 19921207

OTHER SOURCE(S): MARPAT 119:270633

AB (ANH)A1NHCH(CH<sub>2</sub>)pCO<sub>2</sub>H [A, A1 = alkanoyl, alkenoyl, D- or L- $\alpha$ -amino acid residue, XGm<sub>n</sub>; X = NR<sub>1</sub>R<sub>2</sub>, NR<sub>1</sub>C(:NR<sub>2</sub>)NHR<sub>3</sub>, C(:NR<sub>1</sub>)NHR<sub>2</sub>, R<sub>1</sub>-substituted imidazol-1-yl; G = alkanoyl, alkenoyl, (substituted) PhCO, phenylalkanoyl, phenylalkenoyl, etc.; M = NR<sub>4</sub>CH<sub>2</sub>CO; n = 0, 1; p = 1-3; R<sub>1</sub>-R<sub>4</sub> = H, alkyl; with provisos], were prepared Thus, 8-guanidinooctanoic acid was nitrated with fuming HNO<sub>3</sub>/fuming H<sub>2</sub>SO<sub>4</sub> and the product was condensed with aspartic acid amide  $\beta$ -benzyl ester using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride and 1-hydroxybenzotriazole to give N- $\alpha$ -8-(nitroguanidino)octanoylaspartic acid amide  $\beta$ -benzyl ester. This was stirred with iodobenzene bistrifluoroacetate in MeCN/H<sub>2</sub>O to give benzyl N-8-nitroguanidinooctanoyl-3,3-diaminopropionate, which was condensed with 8-nitroguanidinooctanoic acid followed by hydrogenolysis to give N,N'-bis(8-guanidinooctanoyl)-3,3-diaminopropionic acid. This inhibited fibrinogen-mediated platelet aggregation and <sup>125</sup>I-fibrinogen binding to platelets with IC<sub>50</sub>'s of 0.12 and 0.07  $\mu$ M, resp.

L56 ANSWER 50 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:531274 HCAPLUS

DOCUMENT NUMBER: 119:131274

TITLE: The gastrin/cholecystokinin-B receptor antagonist L-365,260 reduces basal acid secretion and prevents gastrointestinal damage induced by aspirin, ethanol and cysteamine in the rat

AUTHOR(S): Pendley, Charles E.; Fitzpatrick, Leo R.; Ewing, Richard W.; Molino, Bruce F.; Martin, Gregory E.

CORPORATE SOURCE: Dep. Pharmacol., Rhone-Poulenc Rorer Cent. Res., Collegeville, PA, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics (1993), 265(3), 1348-54  
 CODEN: JPETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal

LANGUAGE: English

AB L-365,260, a nonpeptide antagonist of gastrin/CCK-B receptors, was evaluated in receptor binding, antisecretory and gastrointestinal damage assays. L-365,260 binds potently and stereo-selectively to gastrin and CCK-B sites in guinea pig tissue. In contrast, L-365,260 binds to the isolated canine parietal cell gastrin receptor weakly, and without stereoselectivity. In the pylorus-ligated rat, low doses of L-365,260, given i.v., attenuated pentagastrin-stimulated acid secretion, whereas higher doses were required to inhibit both histamine-stimulated and basal acid secretion. In an aspirin-induced gastric damage model, L-365,260 was 2.4-fold less potent than the standard histamine H<sub>2</sub> antagonist cimetidine in preventing gastric damage when given i.v., and was 8.3-fold less potent

than cimetidine when give p.o. Moreover, the ED50 value for L-365,260, given i.v., in prevention of aspirin-induced gastric damage (11.5 mg/kg) agreed well with its ED50 value for inhibition of basal acid secretion (12.6 mg/kg). At doses as great as 100 mg/kg p.o., neither L-365,260 nor cimetidine had an effect on ethanol-induced gastric damage. L-365,260, although oral less bioavailable relative to cimetidine in the aspirin gastric damage model, was as potent as cimetidine in the prevention of cysteamine-induced duodenal ulcers in the rat. Thus, the gastrin/CCK-B receptor antagonist L-365,260, at doses supramaximal for the inhibition of pentagastrin-stimulated secretory responses in vivo, inhibits gastrointestinal damage of models of peptic ulcer disease by an antisecretory mechanism of action.

L56 ANSWER 51 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1993:255350 HCAPLUS  
 DOCUMENT NUMBER: 118:255350  
 TITLE: antithrombic peptides and pseudopeptides  
 INVENTOR(S): Klein, Scott I.; **Molino, Bruce F.**; Czekaj, Mark; Gardner, Charles; Becker, Michael R.; Dener, Jeffrey M.; Pelletier, Jeffrey C.  
 PATENT ASSIGNEE(S): Rhone-Poulenc Rorer International (Holdings) Inc., USA  
 SOURCE: PCT Int. Appl., 79 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 4  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9217196	A1	19921015	WO 1992-US2637	19920330
W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2107088	AA	19920929	CA 1992-2107088	19920330
AU 9220143	A1	19921102	AU 1992-20143	19920330
AU 673497	B2	19961114		
EP 577775	A1	19940112	EP 1992-912095	19920330
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 06506699	T2	19940728	JP 1992-511653	19920330
PRIORITY APPLN. INFO.:			US 1991-677006	A2 19910328
			WO 1992-US2637	A 19920330

OTHER SOURCE(S): MARPAT 118:255350

AB Title compds. (>150 compds.) were prepared Thus, polymer-bound Fmoc-Val-OH (Fmoc = 9-fluorenylmethoxycarbonyl) was treated with Fmoc-Asp(CMe<sub>3</sub>)-OH and Fmoc-Arg[SO<sub>2</sub>C<sub>6</sub>H(OMe)Me<sub>3</sub>-4,2,3,6]-OH followed by deprotection to give H-Arg-Asp-Val-OH (I). At 100µM I gave 49% inhibition of fibrinogen-mediated blood platelet aggregation.

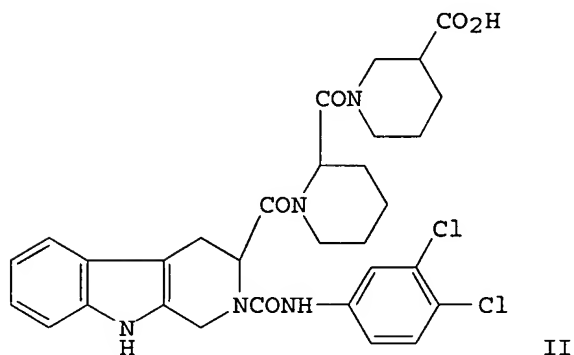
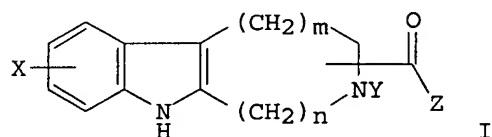
L56 ANSWER 52 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:256054 HCAPLUS  
 DOCUMENT NUMBER: 116:256054  
 TITLE: Preparation of peptide-linked 1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indoles and related compounds as inhibitors of cholecystokinin and gastrin  
 INVENTOR(S): **Molino, Bruce F.**; Darkes, Paul R.; Ewing, William R.  
 PATENT ASSIGNEE(S): Rorer International (Holdings), Inc., USA  
 SOURCE: PCT Int. Appl., 94 pp.

DOCUMENT TYPE: CODEN: PIXXD2  
 LANGUAGE: Patent  
 FAMILY ACC. NUM. COUNT: English  
 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9200295	A1	19920109	WO 1991-US4236	19910613
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5162336	A	19921110	US 1990-573514	19900824
CA 2068887	AA	19911222	CA 1991-2068887	19910613
AU 9186116	A1	19920123	AU 1991-86116	19910613
AU 640277	B2	19930819		
EP 491943	A1	19920701	EP 1991-916717	19910613
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
PRIORITY APPLN. INFO.:			US 1990-542495	A 19900621
			US 1990-573514	A2 19900824
			WO 1991-US4236	A 19910613

OTHER SOURCE(S): MARPAT 116:256054  
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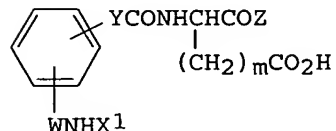


AB Title compds. [I; X = aryl; Y = H, alkyl, (substituted) aralkyl, acyl, aroyl, heterocyclylcarbonyl, carbamoyl, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl; Z = (substituted) N-containing heterocyclyl, amino, amino acid residue, peptide residue, etc.; m = 0-3; n = 0-4], were prepared Thus, (3R)-2-tert-butoxycarbonyl-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole-3-carboxylic acid in THF at -15° was treated with Et<sub>3</sub>N and N,N-bis[2-oxo-3-oxazolinyl]phosphorodiamidic chloride followed by stirring for 20 min. Benzyl N-(L-prolyl)nipecotate was added and the mixture was stirred overnight at ice temperature to give the amide, which was deprotected with CF<sub>3</sub>CO<sub>2</sub>H followed by acylation with 3,4-dichlorophenyl isocyanate and hydrogenolysis to give title compound II. II bound to CCK-A, CCK-B, and gastrin receptors with IC<sub>50</sub>'s of 10, 0.111, and 0.026 μM, resp.

L56 ANSWER 53 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1992:214925 HCAPLUS  
 DOCUMENT NUMBER: 116:214925  
 TITLE: Preparation of (guanidinobenzoyl)dipeptides and related compounds as antithrombotics  
 INVENTOR(S): Klein, Scott I.; Molino, Bruce F.  
 PATENT ASSIGNEE(S): Rorer Pharmaceutical Corp., USA  
 SOURCE: U.S., 6 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5086069	A	19920204	US 1990-475043	19900205
WO 9218117	A1	19921029	WO 1991-US2471	19910411
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
AU 9180896	A1	19921117	AU 1991-80896	19910411
AU 661659	B2	19950803		
EP 584066	A1	19940302	EP 1991-910671	19910411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 08503920	T2	19960430	JP 1991-510398	19910411
PRIORITY APPLN. INFO.:			US 1990-475043	A2 19900205
			WO 1991-US2471	A 19910411
OTHER SOURCE(S):		MARPAT 116:214925		
GI				



AB Title compds. [I; Y = (CH<sub>2</sub>)<sub>n</sub>, CH:CH, XCH<sub>2</sub>; X not defined; Z = NR<sub>1</sub>R<sub>2</sub>, OR<sub>1</sub>; W = (CH<sub>2</sub>)<sub>n</sub> CH:CH(CH<sub>2</sub>)<sub>p</sub>; R<sub>1</sub>, R<sub>2</sub> = alkyl, aryl, aralkyl, allyl; m = 1-3; n = 0-6; p = 0-4; X<sub>1</sub> = H, amidino], were prepared. Thus, L-valine p-alkoxybenzyl alc. resin ester was coupled with N-(9-fluorenylmethoxycarbonyl)aspartic acid β-tert-Bu ester; the product was deprotected with piperidine in DMF followed by condensation with 3-(2-guanidinoethyl)benzoic acid hydrochloride (preparation given) and resin cleavage with CF<sub>3</sub>CO<sub>2</sub>H to give N-(3-(2-guanidinoethyl)benzoyl)aspartylvaline. N-(3-Guanidinomethylbenzoyl)aspartylvaline, prepared similarly, inhibited 125I-fibrinogen binding to platelets with IC<sub>50</sub> = 0.25 μM.

L56 ANSWER 54 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

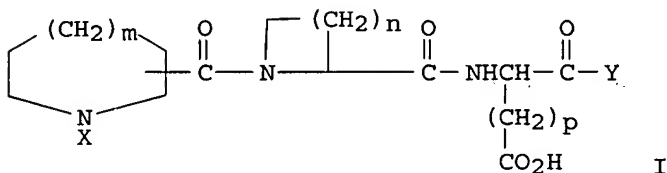
ACCESSION NUMBER: 1992:152412 HCAPLUS  
 DOCUMENT NUMBER: 116:152412  
 TITLE: Preparation of anti-thrombotic peptide and pseudopeptide derivatives  
 INVENTOR(S): Klein, Scott I.; Molino, Bruce F.  
 PATENT ASSIGNEE(S): Rhone-Poulenc Rorer Pharmaceuticals, Inc., USA  
 SOURCE: U.S., 6 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English



FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5064814	A	19911112	US 1990-505286	19900405
US 5328900	A	19940712	US 1992-961216	19921015
PRIORITY APPLN. INFO.:			US 1990-505286	A2 19900405
			US 1991-724675	B1 19910702

OTHER SOURCE(S): MARPAT 116:152412  
GI



AB The title compds. [I; X = H, amidino, COR1; R1 = alkyl, aryl, aralkyl; Y = OR2, NR2R3, naturally occurring L-amino acid residue; R2, R3 = H, alkyl, aryl, aralkyl, allyl; m = 0, 1, 2; n = 0, 1-4 integer; p = 0, 1-3 integer] and their pharmaceutically acceptable salts were prepared  
L-Aspartyl- $\beta$ -tert-Bu ester-L-valine p-alkoxy benzyl resin ester (preparation given) was acylated with (S)-N-(9-fluorenylmethoxycarbonyl)azetidinyl-2-carboxylic acid (preparation given), the resulting (S)-N-(9-fluorenylmethoxycarbonyl)azetidiny-2-carbonyl-L-aspartyl- $\beta$ -tert-Bu ester-L-valine p-alkoxy benzyl resin ester deprotected and then condensed with N-tert-butoxycarbonyl-4-piperidinecarboxylic acid (preparation given), and the resulting resin-bound peptide deprotected and cleaved from the resin by means of CF<sub>3</sub>CO<sub>2</sub>H to give N-[2(S)-1-(piperidin-4-ylcarbonyl)azetidin-5-yl]-L-aspartyl-L-valine. This had an IC<sub>50</sub> of 29.6  $\mu$ M against fibrinogen-mediated platelet aggregation in an in vitro test.

L56 ANSWER 55 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:623777 HCAPLUS

DOCUMENT NUMBER: 115:223777

TITLE: Novel CCK-4 analogs with selectivity for gastrin receptors

AUTHOR(S): Ewing, W. Richard; **Molino, Bruce F.**;  
Pendley, Charles; Darkes, Paul R.; Kosmider, Benidict J.

CORPORATE SOURCE: Cent. Res., Rhone-Poulenc Rorer, King of Prussia, PA, 19406, USA

SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 700-1. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth.  
CODEN: 57HNAI

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The tetrahydro- $\beta$ -carboline replacement for the indole portion of Trp yielded compds. selective for gastrin receptors over cholecystokinin-A receptors.

L56 ANSWER 56 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:598524 HCAPLUS

DOCUMENT NUMBER: 115:198524

TITLE: Anti-thrombotic peptides and pseudopeptides for prophylaxis or treatment of abnormal thrombus formation

INVENTOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles; Pelletier, Jeffrey C.

PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA

SOURCE: PCT Int. Appl., 45 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9104746	A1	19910418	WO 1990-US5448	19900925
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 4952562	A	19900828	US 1989-415006	19890929
AU 9065391	A1	19910428	AU 1990-65391	19900925
AU 646411	B2	19940224		
EP 494248	A1	19920715	EP 1990-915350	19900925
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
JP 05500954	T2	19930225	JP 1990-514349	19900925
PRIORITY APPLN. INFO.:			US 1989-415006	A2 19890929
			US 1990-534385	A 19900607
			WO 1990-US5448	A 19900925

OTHER SOURCE(S): MARPAT 115:198524

AB The invention relates to novel peptides and pseudopeptides and pharmaceutical compns. containing them that inhibit blood platelet aggregation and that are useful for the prophylaxis or treatment of abnormal thrombus formation. Thus, L-ornithylglycyl-L-aspartylvaline (I) was prepared starting from L-valine tert-butyl ester via L-aspartyl- $\beta$ -tert-butyl ester-L-valine  $\alpha$ -tert-butyl ester, glycyl-L-aspartyl- $\beta$ -tert-butyl ester-L-valine  $\alpha$ -tert-butyl ester, N- $\alpha$ -tert-butyloxycarbonyl-N-5-benzyloxycarbonyl-L-ornithylglycyl-L-aspartyl- $\beta$ -tert-butyl ester-L-valine  $\alpha$ -tert-butyl ester, and N- $\alpha$ -tertbutyloxycarbonyl-L-ornithylglycyl-L-aspartyl- $\beta$ -tert-butyl ester-L-valine tert-butyl ester. In vitro tests indicated that the IC50 value of I for inhibition of fibrinogen-mediated platelet aggregation was 15  $\mu$ M. At 100  $\mu$ M I, 80% inhibition was noted.

L56 ANSWER 57 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:598034 HCAPLUS

DOCUMENT NUMBER: 115:198034

TITLE: Novel RGD analogs as antithrombotic agents

AUTHOR(S): Klein, Scott I.; Molino, Bruce F.; Chu, Valeria; Ruggeri, Zaverio; Czekaj, Mark; Gardner, Charles J.; Newman, Jack; Barrett, John A.

CORPORATE SOURCE: Rhone-Poulenc Rorer Cent. Res., King of Prussia, PA, 19453, USA

SOURCE: Pept. 1990, Proc. Eur. Pept. Symp., 21st (1991), Meeting Date 1990, 374-5. Editor(s): Giralt, Ernest; Andreu, David. ESCOM Sci. Publ.: Leiden, Neth.  
CODEN: 57HNAI

DOCUMENT TYPE: Conference

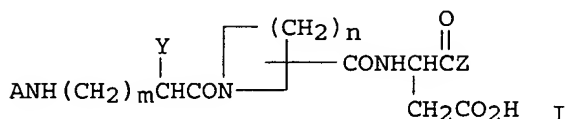
LANGUAGE: English

AB A symposium report with 4 refs.

L56 ANSWER 58 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:583966 HCAPLUS  
 DOCUMENT NUMBER: 115:183966  
 TITLE: Antithrombotic peptides and pseudopeptides  
 INVENTOR(S): Klein, Scott I.; Molino, Bruce F.  
 PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA  
 SOURCE: PCT Int. Appl., 21 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9107976	A1	19910613	WO 1990-US6935	19901128
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
US 5053392	A	19911001	US 1989-444484	19891201
AU 9168900	A1	19910626	AU 1991-68900	19901128
AU 636426	B2	19930429		
EP 502926	A1	19920916	EP 1991-900107	19901128
EP 502926	B1	19960313		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 05504762	T2	19930722	JP 1991-500883	19901128
AT 135367	E	19960315	AT 1991-900107	19901128
PRIORITY APPLN. INFO.:			US 1989-444484	A1 19891201
			WO 1990-US6935	A 19901128
OTHER SOURCE(S):		MARPAT 115:183966		
GI				



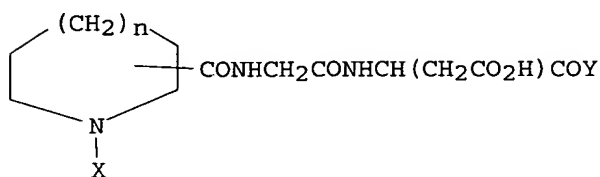
AB The title peptides (I; X = H, amidino, RCO; Y = H, NH<sub>2</sub>, RCONH; Z = NR<sub>1</sub>R<sub>2</sub>, OR<sub>1</sub>, naturally occurring L-amino acid residue; R = alkyl, aryl, aralkyl; R<sub>1</sub>, R<sub>2</sub> = H, alkyl, aryl, aralkyl, allyl; m = 1-5; n = 0-4), which inhibit platelet aggregation and thrombus formation and useful for treatment of thrombogenic diseases, e.g. myocardial infarction and stroke, are prepared. Thus, N-(5-guanidinopentanoyl)azetidine-2(S)-carboxyl-L-aspartyl-L-valine was prepared by the solid phase method and in vitro inhibited fibrinogen-mediated human platelet aggregation with IC<sub>50</sub> of 1.2 μM. Addnl. 4 I were prepared

L56 ANSWER 59 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:583963 HCAPLUS  
 DOCUMENT NUMBER: 115:183963  
 TITLE: Preparation of tripeptide derivatives as antithrombotics  
 INVENTOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.  
 PATENT ASSIGNEE(S): Rorer International (Holdings), Inc., USA  
 SOURCE: PCT Int. Appl., 17 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9105562	A1	19910502	WO 1990-US5367	19900920
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 5051405	A	19910924	US 1989-419305	19891010
AU 9168837	A1	19910516	AU 1991-68837	19900920
PRIORITY APPLN. INFO.:			US 1989-419305	A 19891010
			WO 1990-US5367	A 19900920
OTHER SOURCE(S):		MARPAT 115:183963		
GI				



AB Tripeptide derivs. I (X = H, C(:NH)NH<sub>2</sub>, COR; Y = OH, OR<sub>1</sub>, L-amino acid residue such as Val-OH, Ser-OH, Gly-OH, etc.; R = alkyl, aryl, aralkyl; R<sub>1</sub> = alkyl, aryl, aralkyl, allyl; n = 0-2) were prepared. For example, title compound I (X = (C(:NH)NH<sub>2</sub>, Y = Val-OH, n = 1) (II) was prepared via solid phase methods starting with resin-bound valine and subsequent coupling with Fmoc-Asp(OCMe<sub>3</sub>)-OH, Fmoc-Gly-OH, and N-amidino-4-piperidinecarboxylic acid hydrochloride (preparation given), followed by resin cleavage and deprotection. II at 100 μM showed 92% inhibition of fibrinogen mediated blood platelet aggregation.

L56 ANSWER 60 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1991:24611 HCAPLUS

DOCUMENT NUMBER: 114:24611

TITLE: Preparation of anti-thrombotic peptides and pseudopeptides

INVENTOR(S): Klein, Scott I.; Molino, Bruce F.; Czekaj, Mark; Gardner, Charles J.; Pelletier, Jeffrey C.

PATENT ASSIGNEE(S): Rorer Pharmaceutical Corp., USA

SOURCE: U.S., 9 pp.  
CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4952562	A	19900828	US 1989-415006	19890929
CA 2066047	AA	19910330	CA 1990-2066047	19900925
WO 9104746	A1	19910418	WO 1990-US5448	19900925
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9065391	A1	19910428	AU 1990-65391	19900925
AU 646411	B2	19940224		
EP 494248	A1	19920715	EP 1990-915350	19900925

R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE  
 JP 05500954 T2 19930225 JP 1990-514349 19900925  
 US 5332726 A 19940726 US 1992-859779 19920330  
 PRIORITY APPLN. INFO.: US 1989-415006 A 19890929  
 US 1990-460777 B2 19900104  
 US 1990-534385 A 19900607  
 WO 1990-US5448 A 19900925  
 US 1991-677006 B2 19910328

OTHER SOURCE(S): CASREACT 114:24611; MARPAT 114:24611

AB XCH[(CH<sub>2</sub>)<sub>m</sub>NR<sub>1</sub>Y]ACH<sub>2</sub>BCH(CH<sub>2</sub>CO<sub>2</sub>H)(DCHECO<sub>2</sub>R<sub>2</sub>) (X = H, NR<sub>1</sub>R<sub>2</sub>; Y = H, alkyl, cycloalkyl, aralkyl, COR<sub>2</sub>; A, B, D = CONR<sub>2</sub>; E = H, Me, CHMe<sub>2</sub>; R<sub>1</sub>, R<sub>2</sub> = H, alkyl; m = 2-8; when X = NH<sub>2</sub>, then m = 3, E = CHMe<sub>2</sub>, and ≥1 of A, B, D ≠ CONH), were prepared Thus, H-Arg-Gly-Asp-NHCH<sub>2</sub>CHMe<sub>2</sub>, prepared using fluorenylmethyloxycarbonyl-protected amino acids in the solution phase process, inhibited fibrinogen-mediated platelet aggregation with an IC<sub>50</sub> of 3.6 μM.

L56 ANSWER 61 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1990:96275 HCAPLUS

DOCUMENT NUMBER: 112:96275

TITLE: Endothelium-dependent vascular responses: effect of hypertension and cyclosporin A

AUTHOR(S): Luescher, T. F.; Yang, Z.; Diederich, D.; Buehler, F. R.

CORPORATE SOURCE: Dep. Med., Univ. Hosp., Basel, Switz.

SOURCE: Zeitschrift fuer Kardiologie (1989), 78(Suppl. 6), 132-6

CODEN: ZKRDAX; ISSN: 0300-5860

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with 39 refs. Through the release of endothelium-derived relaxing and contracting factors, the endothelium can profoundly affect local vascular tone. In hypertension and during chronic cyclosporin A therapy, morphol. changes of the endothelium develop. This review summarizes functional alterations of the endothelium under these conditions.

L56 ANSWER 62 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:173247 HCAPLUS

DOCUMENT NUMBER: 110:173247

TITLE: Preparation of heteroarene-fused diazacycloalkanones as cardiotonics

INVENTOR(S): Spada, Alfred P.; Campbell, Henry F.; Kuhla, Donald E.; Studt, William L.; Faith, William C.; Molino, Bruce F.

PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA

SOURCE: PCT Int. Appl., 57 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

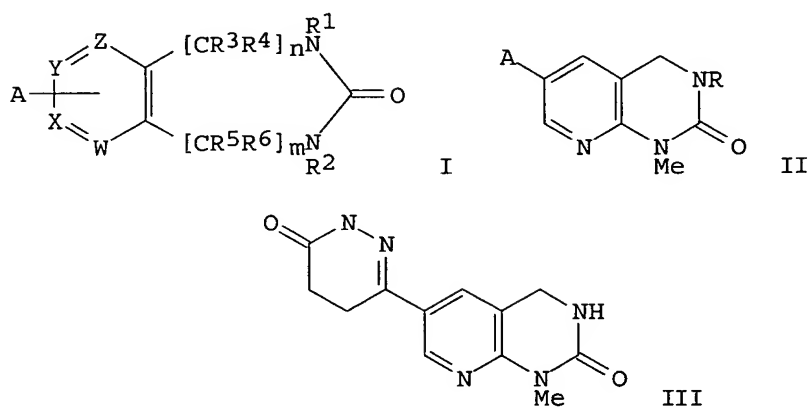
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8803025	A1	19880505	WO 1987-US2879	19871027
W: AU, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4859672	A	19890822	US 1986-925008	19861029
AU 8782327	A1	19880525	AU 1987-82327	19871027

EP 333727                      A1            19890927            EP 1987-907490            19871027  
 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE  
 JP 02500518                    T2            19900222            JP 1987-506948            19871027  
 US 5002944                    A            19910326            US 1989-350366            19890511  
 PRIORITY APPLN. INFO.:            US 1986-925008            A            19861029  
    WO 1987-US2879            A            19871027  
 OTHER SOURCE(S):            CASREACT 110:173247; MARPAT 110:173247  
 GI



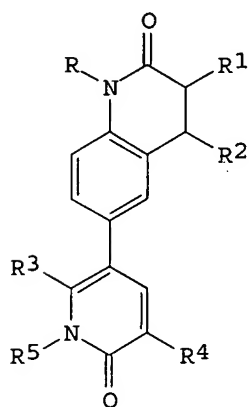
AB    The title compds. [I; A = (un)substituted 2-pyridon-5-yl, 3-pyridazon-6-yl, 4-pyrimidon-6-yl, pyrimidine-2,4-dion-6-yl; 1 or 2 of W, X, Y, Z = N, the others = CR7, CR8, CR9; R1-R9 = H, alkyl, aryl, aralkyl; R7-R9 may addnl. bond with A; R3R4, R5R6 = O; m, n = 0,1] were prepared as cardiotonics (no data). 3-(Aminomethyl)-2-(methylamino)pyridine (preparation given) was refluxed 6 h with 1,1'-carbonyldiimidazole to give pyridopyrimidinone II (A = R = H) which was converted in 4 steps to II (A = Me3Sn, R = Ac). To latter was converted to II (A = COCH2CH2CO2Me, R = Ac) which was refluxed 8h with N2H4.H2O in EtOH to give title compound III.

L56 ANSWER 63 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:            1989:173107 HCAPLUS  
 DOCUMENT NUMBER:            110:173107  
 TITLE:                        6-(6-Alkylpyridone)carbostyryl compounds and their use  
                                  as inotropics  
 INVENTOR(S):                Campbell, Henry F.; Kuhla, Donald E.; **Molino,**  
                                  **Bruce F.**; Studdt, William L.  
 PATENT ASSIGNEE(S):        Rorer International (Overseas), Inc., USA  
 SOURCE:                        PCT Int. Appl., 27 pp.  
                                  CODEN: PIXXD2  
 DOCUMENT TYPE:                Patent  
 LANGUAGE:                    English  
 FAMILY ACC. NUM. COUNT:    1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8800188	A1	19880114	WO 1987-US1489	19870618
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4785005	A	19881115	US 1986-878123	19860625
AU 8776494	A1	19880129	AU 1987-76494	19870618
EP 311634	A1	19890419	EP 1987-904350	19870618

R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE  
 JP 01503456 T2 19891122 JP 1987-503968 19870618  
 PRIORITY APPLN. INFO.: US 1986-878123 A2 19860625  
 WO 1987-US1489 A 19870618  
 OTHER SOURCE(S): MARPAT 110:173107  
 GI



AB Title compds. I (R-R3, R5 = H, alkyl; R4 = alkyl, alkoxyalkyl, hydroxyalkyl, cyano, carbamoyl, alkylcarbamoyl, CHO, alkyleneamino, NH2, halo) or their salts, useful as pos. inotropics, are prepared 6-(2-Bromopropionyl)-3,4-dihydrocarbostyryl was treated with KOAc and HOAc at reflux for 5 h to give the acetoxy derivative, which was reduced with NaBH4 in diglyme to give 6-(2-acetoxy-1-hydroxypropyl)-3,4-dihydrocarbostyryl. The latter compound was dehydrated and hydrolyzed to 6-(2-oxopropyl)-3,4-dihydrocarbostyryl, which was condensed with Me2NCH(OMe)2 to give 6-[1-(dimethylamino)-3-oxo-1-buten-2-yl]-3,4-dihydrocarbostyryl. This compound was treated with 2-cyanoacetamide and NaH in DMF to give I (R-R2 = R5 = H, R3 = Me, R4 = cyano) (II). In the ganglionic-β blocked dog test, II at 30 µg/kg i.v. increased the contractile force by 97%, heart rate by 17%, and aortic blood flow by 51% with no change in arterial blood pressure. In contrast, milrinone (a known inotropic) at 100 µg increased contractile force by 111%, heart rate 19%, and aortic blood flow only transiently, while decreasing arterial blood pressure by 32%.

L56 ANSWER 64 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1989:75899 HCAPLUS

DOCUMENT NUMBER: 110:75899

TITLE: Synthetic and mechanistic studies based on pyrolysis products

AUTHOR(S): Fraser-Reid, B.; Cusmano, John; Lowe, Derek;  
**Molino, Bruce**; Mootoo, David; Underwood,  
 Russell; Farrell, Thomas; Khadem, John

CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC,  
 27706, USA

SOURCE: F.E.C.S. Int. Conf. Chem. Biotechnol. Biol. Act. Nat.  
 Prod., [Proc.], 3rd (1987), Meeting Date 1985, Volume  
 1, 180-94. VCH: Weinheim, Fed. Rep. Ger.

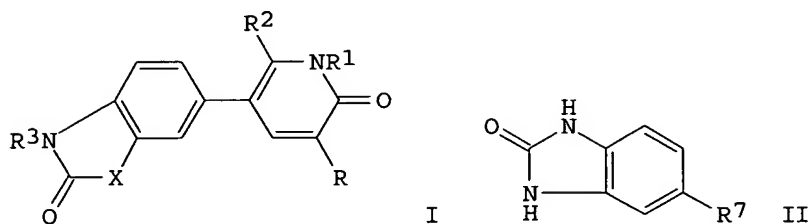
CODEN: 56IAAB

DOCUMENT TYPE: Conference

LANGUAGE: English  
 AB A conference report on synthetic and mechanistic studies based on the pyrolysis products of the title polysaccharides.

L56 ANSWER 65 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1988:493054 HCAPLUS  
 DOCUMENT NUMBER: 109:93054  
 TITLE: Preparation of pyridonylbenzazinones and analogs as cardiotonics  
 INVENTOR(S): Molino, Bruce F.; Campbell, Henry F.; Kuhla, Donald E.; Studt, William L.  
 PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA  
 SOURCE: PCT Int. Appl., 41 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8801508	A1	19880310	WO 1987-US2007	19870813
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4764512	A	19880816	US 1986-900868	19860827
AU 8780303	A1	19880324	AU 1987-80303	19870813
EP 323479	A1	19890712	EP 1987-906236	19870813
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02501302	T2	19900510	JP 1987-505653	19870813
PRIORITY APPLN. INFO.:			US 1986-900868	A2 19860827
			WO 1987-US2007	A 19870813
OTHER SOURCE(S):			CASREACT 109:93054; MARPAT 109:93054	
GI				

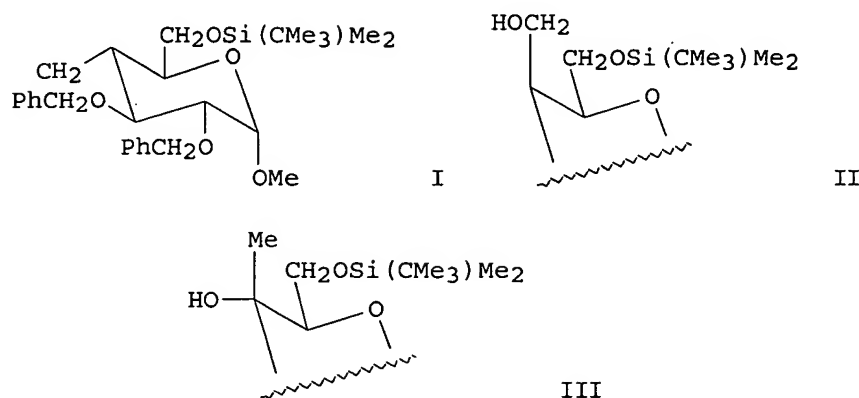


AB The title compds. [I; R = H, halo, cyano, NH<sub>2</sub>, H<sub>2</sub>NCO, alkyl, etc.; X = (CR<sub>4</sub>R<sub>5</sub>)aNR<sub>6</sub>(CR<sub>4</sub>R<sub>5</sub>)b; R<sub>1</sub>-R<sub>3</sub>, R<sub>5</sub> = H, alkyl; R<sub>4</sub>, R<sub>6</sub> = R<sub>1</sub>, aralkyl; a, b = 0-2; a + b = 0-2] were prepared as cardiotonics (no data).  
 Dihydrobenzimidazole II (R<sub>2</sub> = MeCHBrCO) (preparation given) was stirred 4 h with NaBH<sub>4</sub> in MeOH containing NaOH to give II [R<sub>7</sub> = MeOCHMeCH(OH)] which was refluxed 48 h in EtOAc with repeated addns. of 4-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H to give II (R<sub>7</sub> = MeCOCH<sub>2</sub>). The latter was heated at 70° for 22 h with (MeO)<sub>2</sub>HCHNMe<sub>2</sub> and pyridine to give II (R<sub>7</sub> = Me<sub>2</sub>NCH:CCOMe) which was added to H<sub>2</sub>NCOCH<sub>2</sub>CN in DMF previously treated with NaH and the mixture stirred 24 h to give I (R = cyano, R<sub>1</sub> = R<sub>3</sub> = H, R<sub>2</sub> = Me, X = NH).

L56 ANSWER 66 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1988:204910 HCAPLUS  
 DOCUMENT NUMBER: 108:204910



TITLE: Stereoselectivity in the hydroboration of C4-C-methylene groups  
 AUTHOR(S): Molino, Bruce F.; Cusmano, John; Mootoo, David R.; Faghih, Ramine; Fraser-Reid, Bert  
 CORPORATE SOURCE: Dep. Chem., Duke Univ., Durham, NC, 27706, USA  
 SOURCE: Journal of Carbohydrate Chemistry (1987), 6(3), 479-93  
 CODEN: JCACDM; ISSN: 0732-8303  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 108:204910  
 GI



AB Conditions for the hydroxylation of an exocyclic methylene group at C-4 of a pyranoside ring via hydroboration were examined with a view to determining the optimum procedure for obtaining the axially-oriented C(4)-CH<sub>2</sub>OH group. The regio- and stereochem. outcome of the reactions depend not only on the hydroborating reagent used, but, to a surprising degree, on the nature of the protecting group at the remote C(6)-OH. Silyl ethers are preferred because the only byproduct formed is the tertiary alc., which can be recycled through dehydration to the starting alkene with SOCl<sub>2</sub>. Thus, C-methylene hexopyranoside I was treated with BH<sub>3</sub> in THF and then with aqueous NaOH and H<sub>2</sub>O<sub>2</sub> to give 40% hydroxymethyl derivative II and 25% alc. III.

L56 ANSWER 67 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1988:56472 HCAPLUS  
 DOCUMENT NUMBER: 108:56472  
 TITLE: Pyranosidic homologation. VII. Controlled formation of dipyranoside derivatives through carbon 6 and oxygen 4  
 AUTHOR(S): Molino, Bruce Francis; Fraser-Reid, Bert  
 CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA  
 SOURCE: Canadian Journal of Chemistry (1987), 65(12), 2834-42  
 CODEN: CJCHAG; ISSN: 0008-4042  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 108:56472  
 GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB A procedure was developed for pyranosidic homologation of Me  $\alpha$ -D-glucopyranoside via C(4) and C(6). Reaction of the aldehyde group of hexodialdopyranoside I with the Wittig-Bestmann reagent, Ph<sub>3</sub>P:CHCH(OEt)<sub>2</sub>, gave an E/Z mixture of acetals, II, which cyclized under the specific catalysis of pyridinium p-toluenesulfonate and in the presence of alcs. to give anomERICALLY pure olefinic bipyranosides, III [R = Me, PhCH<sub>2</sub>, 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 3,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>]. A general procedure for epoxidn. of the latter involved OsO<sub>4</sub> hydroxylation, followed by reaction with phosgene iminium chloride (Viehe's salt) to give chlorocarbamates IV and V, which were then subjected to the action of sodium methoxide. This allowed for the formation of a single series of diastereomeric epoxides, VI, and controlled cleavage of VI with nucleophiles then followed well-established precedents. Selective access to the "ends" of VI [R = 4-MeOC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>, 3,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>] were obtained by oxidative removal of the activated benzyl glycosides with DDQ.

L56 ANSWER 68 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1988:6037 HCAPLUS

DOCUMENT NUMBER: 108:6037

TITLE: Preparation of benzodiazinone-pyridazinones and hydroxypyrazole compounds as cardiotonics  
INVENTOR(S): Kuhla, Donald Ernest; Campbell, Henry Flud; Studdt, William Lyon; Faith, William Cass; **Molino, Bruce Francis**

PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA

SOURCE: PCT Int. Appl., 68 pp.

CODEN: PIXXD2

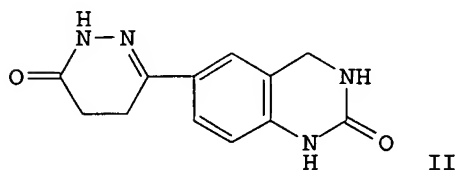
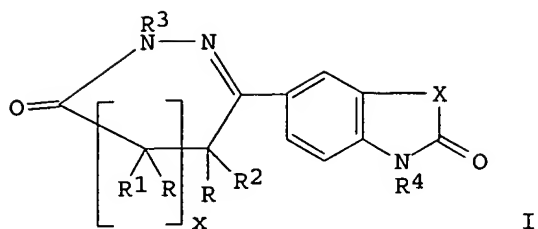
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8703201	A1	19870604	WO 1986-US2497	19861120
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4725686	A	19880216	US 1985-800986	19851122
AU 8767385	A1	19870701	AU 1987-67385	19861120
AU 600249	B2	19900809		
EP 247177	A1	19871202	EP 1987-900392	19861120
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 63502030	T2	19880811	JP 1987-500197	19861120
CA 1276145	A1	19901113	CA 1986-523546	19861121
US 4785101	A	19881115	US 1987-63481	19870617
US 4868300	A	19890919	US 1987-102083	19870721
US 4906630	A	19900306	US 1988-255664	19881011
PRIORITY APPLN. INFO.:			US 1985-800986	A2 19851122
			WO 1986-US2497	A 19861120
			US 1987-63481	A3 19870617
OTHER SOURCE(S):	CASREACT 108:6037; MARPAT 108:6037			
GI				



AB The title compds. [I; X = (CR5R6)aNR7(CR5R6)b; R, R2-R7 = H, alkyl, aralkyl; R2 = (un)substituted C1-3 alkyl; R2,R52, R6R7 = bond; R5R6 = C2-5 alkylene; a + b = 0-2; x = 0, 1] and their pharmaceutically acceptable salts were prepared as pos. inotropic agents, useful in treating congestive heart failure (no data). 3,4-Dihydro-2(1H)-quinazolinone underwent Friedel-Crafts acylation by refluxing in CS<sub>2</sub> with MeO<sub>2</sub>CCH<sub>2</sub>CH<sub>2</sub>COCl and AlCl<sub>3</sub> to give 6-(3-carboxypropionyl)-3,4-dihydro-2(1H)-quinazolinone. This was refluxed in EtOH with N<sub>2</sub>H<sub>4</sub>.H<sub>2</sub>O to give (oxypyridazinyl)quinazolinone II.

L56 ANSWER 69 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:598793 HCAPLUS

DOCUMENT NUMBER: 107:198793

TITLE: Tripyranoside precursors for ansamycins. Pyranosidic homologation. 6

AUTHOR(S): Fraser-Reid, Bert; Molino, Bruce F.;

Magdzinski, Leon; Mootoo, David R.

CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA

SOURCE: Journal of Organic Chemistry (1987), 52(20), 4505-11

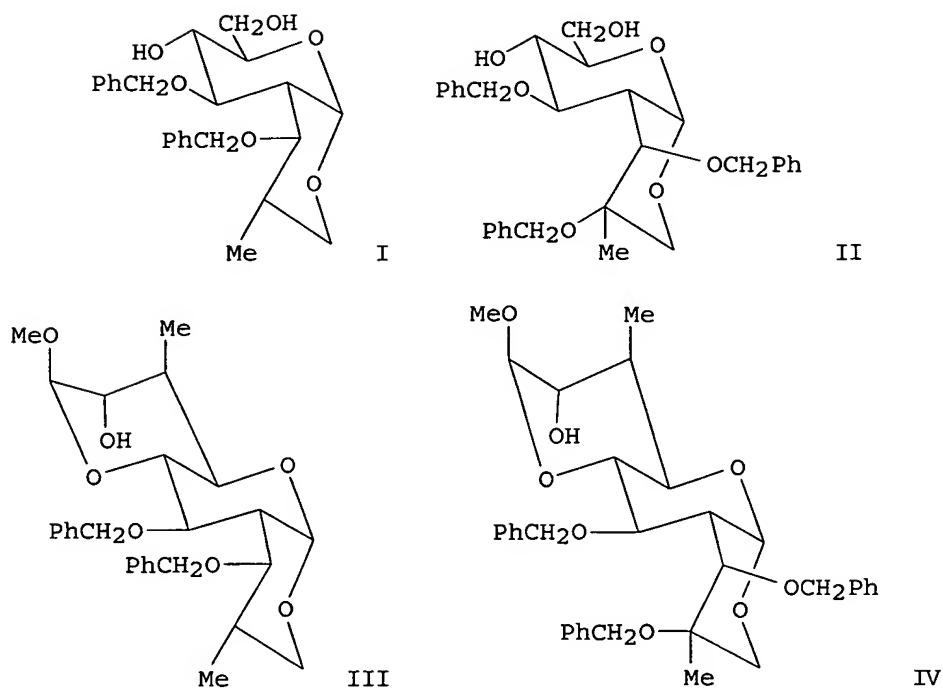
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 107:198793

GI



AB The primary and secondary alcs. of the dipyranses I and II were used as implements for elaborating the upper pyranoside rings of the tripyranoses III and IV, resp. III contains seven of the eight chiral centers of rifamycin S, while IV fixes seven of the nine chiral centers of streptovaricin A. For the synthetic procedures, the primary alc. was oxidized to an aldehyde, which was subjected to olefination with a phosphorane of the type  $\text{PH}_3\text{P}:\text{CHCH}(\text{OR})_2$ . Treatment with pyridinium p-toluenesulfonate, specifically, in the presence of an alc. caused cyclization with the secondary alc., resulting in a hexenopyranoside, which was glycosidated in situ by the alc. The resulting hexenopyranoside was then epoxidized, by a new procedure that involved hydroxylation with  $\text{OsO}_4$  and treatment of the cis diol so formed with phosgene iminium chloride (Viehe's salt) to give a chloro carbamate, which then reacted with methoxide to give the desired epoxide. Opening of the ring with  $\text{Me}_2\text{Mg}$  then completed the requirements for the upper ring.

L56 ANSWER 70 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:554621 HCAPLUS

DOCUMENT NUMBER: 107:154621

TITLE: Dipyranoside precursors for ansamycins. Pyranosidic homologation. 5

AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; Molino, Bruce F.; Mootoo, David R.

CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC, 27706, USA

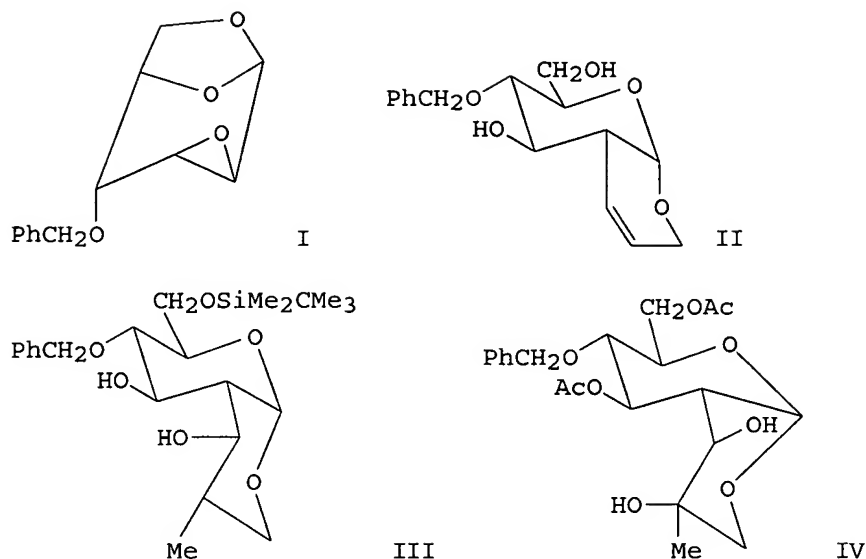
SOURCE: Journal of Organic Chemistry (1987), 52(20), 4495-504  
CODEN: JOCEAH; ISSN: 0022-3263

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 107:154621

GI



AB The process of pyranosidic homologation was applied to the readily obtainable dianhydro sugar I in the context of preparation of precursors for mols. containing multiple contiguous chiral centers (e.g., the ansa chains of rifamycin S and streptovaricin A). Two approaches for construction of the lower satellites were determined. The first involved opening of the epoxide I with a carbanion derived from propargyl alc., followed by Lindlar reduction. Treatment of the resulting allylic alc. with  $\text{CF}_3\text{CO}_2\text{H}$  lead to internal glycosidation; the cis-fused (i.e.,  $\alpha$ ) bicyclic system II being highly favored. II on sequential silylation, epoxidn., epoxide ring cleavage with  $\text{LiMe}_2\text{C}_4$ , pyridinium chlorochromate oxidation, and  $\text{LiAlH}_4$  reduction gave III the precursor for rifamycin S. Also prepared from I was IV, required for streptovaricin A.

L56 ANSWER 71 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1987:496711 HCAPLUS

DOCUMENT NUMBER: 107:96711

TITLE: Preparation of hydroxy- and aminothiazolylbenzodiazinones as cardiotoxic agents  
INVENTOR(S): Kubla, Donald E.; Campbell, Henry F.; Studt, William L.; Molino, Bruce F.; Tucker, Thomas J.

PATENT ASSIGNEE(S): William H. Rorer, Inc., USA

SOURCE: U.S., 12 pp.  
CODEN: USXXAM

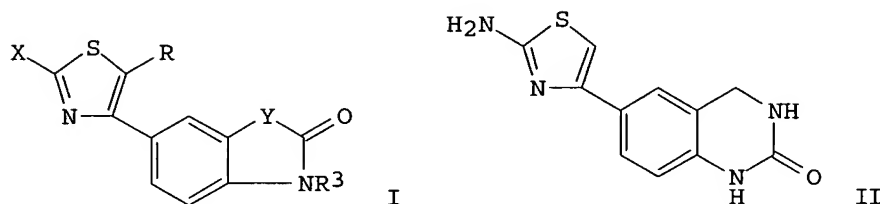
DOCUMENT TYPE: Patent  
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

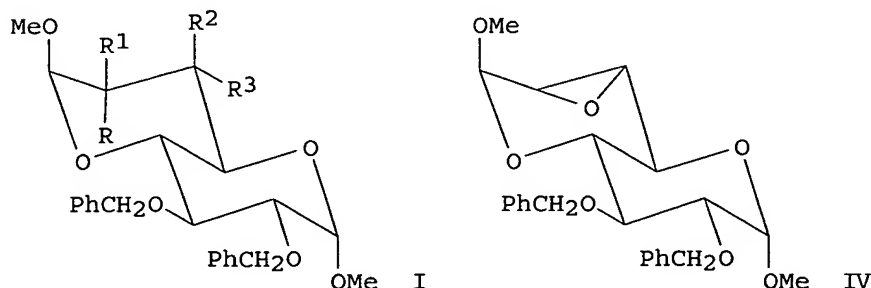
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4666913	A	19870519	US 1985-801071	19851122
WO 8703199	A1	19870604	WO 1986-US2496	19861120
W: AU, JP				

RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE  
 AU 8767386 A1 19870701 AU 1987-67386 19861120  
 AU 582982 B2 19890413  
 EP 247167 A1 19871202 EP 1987-900025 19861120  
 R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE  
 JP 63502031 T2 19880811 JP 1987-500198 19861120  
 PRIORITY APPLN. INFO.: US 1985-801071 A 19851122  
 WO 1986-US2496 A 19861120  
 OTHER SOURCE(S): CASREACT 107:96711; MARPAT 107:96711  
 GI



AB The title compds. [I; X = NR<sub>1</sub>R<sub>2</sub>, OH; Y = (CR<sub>4</sub>R<sub>5</sub>)aNR<sub>6</sub>(CR<sub>4</sub>R<sub>5</sub>)b; a, b = 0-2, a + b ≤ 2; R, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, R<sub>6</sub> = H, alkyl, aralkyl; adjacent R<sub>4</sub> groups may be double bond; R<sub>4</sub>R<sub>5</sub> may be (CH<sub>2</sub>)<sub>d</sub>; d = 2-5] are prepared as cardiotonic agents (no data). Friedel-Crafts acylation of 2.6 g 3,4-dihydro-2(1H)-quinazolinone by 6.2 g BrCH<sub>2</sub>COCl in refluxing CS<sub>2</sub> with AlCl<sub>3</sub> catalyst gave the crude 6-(bromoacetyl) derivative, which (3 g) underwent cyclocondensation with 0.9 g thiourea in refluxing EtOH to give (aminothiazolyl)quinazolinone derivative II.

L56 ANSWER 72 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN  
 ACCESSION NUMBER: 1987:440203 HCAPLUS  
 DOCUMENT NUMBER: 107:40203  
 TITLE: A ready route from vicinal cis-diols to epoxides  
 AUTHOR(S): Sunay, Ustun; Mootoo, David; Molino, Bruce;  
 Fraser-Reid, Bert  
 CORPORATE SOURCE: Paul M. Gross Chem. Lab., Duke Univ., Durham, NC,  
 27706, USA  
 SOURCE: Tetrahedron Letters (1986), 27(39), 4697-700  
 CODEN: TELEAY; ISSN: 0040-4039  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 OTHER SOURCE(S): CASREACT 107:40203  
 GI



AB A two-step procedure for converting a vicinal cis-diol into epoxides is described which involves the preparation of chlorocarbamate intermediate by the use of  $\text{Me}_2\text{R}_1^+:\text{CCl}_2\text{Cl}^-$ . For example, treatment of diol (I;  $\text{R} = \text{R}_3 = \text{OH}$ ,  $\text{R}_1 = \text{R}_2 = \text{H}$ ) with  $\text{Me}_2\text{N}^+:\text{CCl}_2\text{Cl}^-$  in  $\text{CH}_2\text{Cl}_2$  in the presence of  $\text{Et}_3\text{N}$  at reflux gave chlorocarbamates [I;  $\text{R} = \text{Me}_2\text{NCO}_2$ ,  $\text{R}_1 = \text{R}_3 = \text{H}$ ,  $\text{R}_2 = \text{Cl}$  (II);  $\text{R} = \text{R}_2 = \text{H}$ ,  $\text{R}_1 = \text{Cl}$ ,  $\text{R}_3 = \text{Me}_2\text{NCO}_2$  (III)] in 82 and 5% yield, resp. Treatment of II with  $\text{NaOMe}$  gave 70% epoxide IV. III did not react with  $\text{NaOMe}$ .

L56 ANSWER 73 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:626538 HCAPLUS

DOCUMENT NUMBER: 105:226538

TITLE: Bicyclic heteroaryl thiazole compounds and their cardiotonic uses

INVENTOR(S): Kuhla, Donald Ernest; Campbell, Henry Flud; Studt, William Lyon; **Molino, Bruce Francis**

PATENT ASSIGNEE(S): Rorer International (Overseas), Inc., USA

SOURCE: PCT Int. Appl., 54 pp.

CODEN: PIXXD2

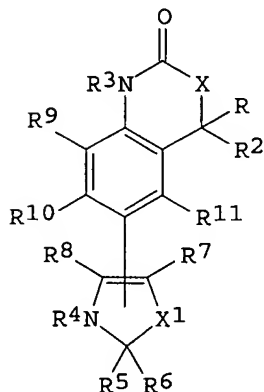
DOCUMENT TYPE: Patent

LANGUAGE: English

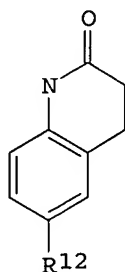
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8603749	A1	19860703	WO 1985-US2522	19851218
W: AU, JP, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
US 4721721	A	19880126	US 1984-683204	19841218
AU 8652388	A1	19860722	AU 1986-52388	19851218
EP 207140	A1	19870107	EP 1986-900535	19851218
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 62501417	T2	19870611	JP 1986-500472	19851218
US 4818755	A	19890404	US 1986-897064	19860728
PRIORITY APPLN. INFO.:			US 1984-683204	A2 19841218
			CA 1985-497858	A 19851217
			WO 1985-US2522	A 19851218
OTHER SOURCE(S):			CASREACT 105:226538; MARPAT 105:226538	
GI				



I



II

AB Title compds. I [X = bond, CR:CR, CRR1, CRR2CRR2; X1 = N, S; R, R3, R7, R8 = H, alkyl; R1 = H, alkyl, OH, amino, acetamido; R2 = H, alkyl; R1R2 = bond; RR2 = (CH2)2-5; R4R5 = bond; NR4CR5 = imidazo; R6 = H, (substituted) alkyl, aryl, amino, amidino, OH, N-containing heterocycle; R9-R11 = H, alkyl, alkoxy, OH, alkylthio, alkylsulfinyl, alkylsulfonyl], useful for the treatment of congestive heart disease (no data), were prepared Thus, PhNH2 reacted with ClCH2CH2COCl to give ClCH2CH2CONHPh, which cyclized in the presence of AlCl3 to give quinolinone II (R12 = H), which was treated with ClCH2COCl-AlCl3 to form II (R12 = COCH2Cl). This cyclized on reaction with H2NCSNH2 to give II (R12 = 2-aminothiazol-4-yl).

L56 ANSWER 74 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1986:149285 HCAPLUS

DOCUMENT NUMBER: 104:149285

TITLE: Pyranosidic homologation a carbohydrate approach to the synthesis of the ansa chains of streptovaricin A and rifamycin S

AUTHOR(S): **Molino, Bruce Francis**

CORPORATE SOURCE: Univ. Maryland, College Park, MD, USA

SOURCE: (1984) 233 pp. Avail.: Univ. Microfilms Int., Order No. DA8510266

From: Diss. Abstr. Int. B 1985, 46(3), 844

DOCUMENT TYPE: Dissertation

LANGUAGE: English

AB Unavailable

L56 ANSWER 75 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:175150 HCAPLUS

DOCUMENT NUMBER: 100:175150

TITLE: Pyranosidic homologation: Part I: Extending the carbohydrate template via C6 and C4

AUTHOR(S): **Molino, Bruce F.**; Magdzinski, Leon; Fraser-Reid, Bert

CORPORATE SOURCE: Dep. Chem., Univ. Maryland, College Park, MD, 20742, USA

SOURCE: Tetrahedron Letters (1983), 24(52), 5819-22

CODEN: TELEAY; ISSN: 0040-4039

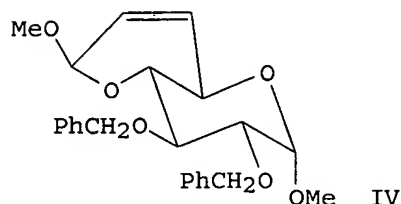
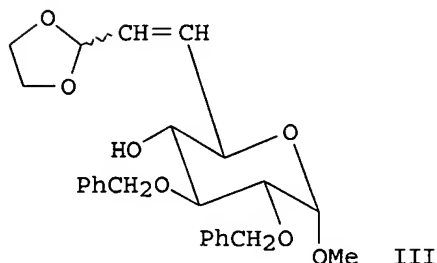
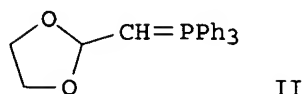
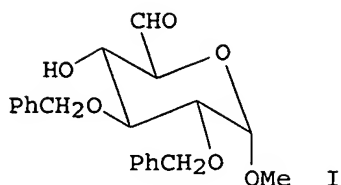
DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 100:175150

GI





AB The aldehyde I reacts with ylide (II) to give III as a 4:1 Z/E mixture which, upon methanolysis under catalysis by pyridinium p-toluenesulfonate, affords the bispyranoside IV as a single anomer.

L56 ANSWER 76 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:68612 HCAPLUS

DOCUMENT NUMBER: 100:68612

TITLE: New strategy for carbohydrate-based syntheses of multichiral arrays: pyranosidic homologation. 2

AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; **Molino, Bruce**

CORPORATE SOURCE: Chem. Dep., Univ. Maryland, College Park, MD, 20742, USA

SOURCE: Journal of the American Chemical Society (1984), 106(3), 731-4

CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A process of pyranosidic homologation has been developed whereby 'satellite' pyranosides are attached to the front and rear of a 'backbone' pyranoside. The resulting manifold has capacity for eight contiguous chiral centers, two of which survive from the starting levoglucosan. The other six are introduced rationally and with complete stereo- and/or regioselectivity in each case, and configurational assignments are readily made by 200-MHz <sup>1</sup>H NMR. The study is outlined with respect to a key intermediate for the ansa chain of rifamycin, but the general applicability to other pseudo higher carbon sugars, as well as their authentic counterparts, is clearly obvious.

L56 ANSWER 77 OF 77 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1983:405905 HCAPLUS

DOCUMENT NUMBER: 99:5905

TITLE: Carbohydrate derivatives in the asymmetric synthesis of natural products

AUTHOR(S): Fraser-Reid, Bert; Magdzinski, Leon; **Molino, Bruce**

CORPORATE SOURCE: Chem. Dep., Univ. Maryland, College Park, MD, 20742, USA

SOURCE: Curr. Trends Org. Synth., Proc. Int. Conf., 4th (1983)

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, Meeting Date 1982, 197-204. Editor(s): Nozaki,  
Hitosi. Pergamon: Oxford, UK.  
CODEN: 49OPAS

DOCUMENT TYPE: Conference; General Review  
LANGUAGE: English

AB A review with 30 refs.

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S.